#4

FIG. 1A

```
   1  agggagaggc agtgaccatg aaggctgtgc tgcttgccct gttgatggca
  51  ggcttggccc tgcagccagg cactgccctg ctgtgctact cctgcaaagc
 101  ccaggtgagc aacgaggact gcctgcaggt ggagaactgc acccagctgg
 151  gggagcagtg ctggaccgcg cgcatccgcg cagttggcct cctgaccgtc
 201  atcagcaaag gctgcagctt gaactgcgtg gatgactcac aggactacta
 251  cgtgggcaag aagaacatca cgtgctgtga caccgacttg tgcaacgcca
 301  gcggggccca tgccctgcag ccggctgccg ccatccttgc gctgctccct
 351  gcactcggcc tgctgctctg gggacccggc cagctatagg ctctgggggg
 401  ccccgctgca gcccacactg ggtgtggtgc cccaggcctt tgtgccactc
 451  ctcacagaac ctggcccagt gggagcctgt cctggttcct gaggcacatc
 501  ctaacgcaag tttgaccatg tatgtttgca ccccttttcc ccnaaccctg
 551  accttcccat gggccttttc caggattccn accnggcaga tcagttttag
 601  tganacanat ccgcntgcag atggcccctc caaccntttn tgttgntgtt
 651  tccatggccc agcattttcc acccttaacc ctgtgttcag gcacttnttc
 701  ccccaggaag ccttccctgc ccaccccatt tatgaattga gccaggtttg
 751  gtccgtggtg tcccccgcac ccagcagggg acaggcaatc aggagggccc
 801  agtaaaggct gagatgaagt ggactgagta gaactggagg acaagagttg
 851  acgtgagttc ctgggagttt ccagagatgg ggcctggagg cctggaggaa
 901  ggggccaggc ctcacatttg tggggntccc gaatggcagc ctgagcacag
 951  cgtaggccct taataaacac ctgttggata agccaaaaaa aaaaaaaa
```

FIG. 1B

MKAVLLALLMAGLALQPGTALLCYSCKAQVSNEDCLQV

ENCTQLGEQCWTARIRAVGLLTVISKGCSLNCVDDS

QDYYVGKKNITCCDTDLCNASGAHALQPAAAILALLPAL

GLLLWGPGQL

FIG. 2

```
    ATGAAGACAGTTTTTTTTATCCTGCTGGCCACCTACTTAGCCCTGCATCCAGGTGCTGCT
1   ---------+---------+---------+---------+---------+---------+ 60
    TACTTCTGTCAAAAAAAATAGGACGACCGGTGGATGAATCGGGACGTAGGTCCACGACGA

    M  K  T  V  F  F  I  L  L  A  T  Y  L  A  L  H  P  G  A  A

    CTGCAGTGCTATTCATGCACAGCACAGATGAACAACAGAGACTGTCTGAATGTACAGAAC
61  ---------+---------+---------+---------+---------+---------+ 120
    GACGTCACGATAAGTACGTGTCGTGTCTACTTGTTGTCTCTGACAGACTTACATGTCTTG

    L  Q  C  Y  S  C  T  A  Q  M  N  N  R  D  C  L  N  V  Q  N

    TGCAGCCTGGACCAGCACAGTTGCTTTACATCGCGCATCCGGGCCATTGGACTCGTGACA
121 ---------+---------+---------+---------+---------+---------+ 180
    ACGTCGGACCTGGTCGTGTCAACGAAATGTAGCGCGTAGGCCCGGTAACCTGAGCACTGT

    C  S  L  D  Q  H  S  C  F  T  S  R  I  R  A  I  G  L  V  T

    GTTATCAGTAAGGGCTGCAGCTCACAGTGTGAGGATGACTCGGAGAACTACTATTTGGGC
181 ---------+---------+---------+---------+---------+---------+ 240
    CAATAGTCATTCCCGACGTCGAGTGTCACACTCCTACTGAGCCTCTTGATGATAAACCCG

    V  I  S  K  G  C  S  S  Q  C  E  D  D  S  E  N  Y  Y  L  G

    AAGAAGAACATCACGTGCTGCTACTCTGACCTGTGCAATGTCAACGGGGCCCACACCCTG
241 ---------+---------+---------+---------+---------+---------+ 300
    TTCTTCTTGTAGTGCACGACGATGAGACTGGACACGTTACAGTTGCCCCGGGTGTGGGAC

    K  K  N  I  T  C  C  Y  S  D  L  C  N  V  N  G  A  H  T  L

    AAGCCACCCACCACCCTGGGGCTGCTGACCGTGCTCTGCAGCCTGTTGCTGTGGGGCTCC
301 ---------+---------+---------+---------+---------+---------+ 360
    TTCGGTGGGTGGTGGGACCCCGACGACTGGCACGAGACGTCGGACAACGACACCCCGAGG

    K  P  P  T  T  L  G  L  L  T  V  L  C  S  L  L  L  W  G  S

    AGCCGTCTGTAGGCTCTGGGAGAGCCTACCATAGCCCGATTGTGAAGGGATGAGCTGCAC
361 ---------+---------+---------+---------+---------+---------+ 420
    TCGGCAGACATCCGAGACCCTCTCGGATGGTATCGGGCTAACACTTCCCTACTCGACGTG

    S  R  L  *

    TCCACCCCACCCCCACACAGG
421 ---------+---------+- 441
    AGGTGGGGTGGGGGTGTGTCC
```

FIG. 3

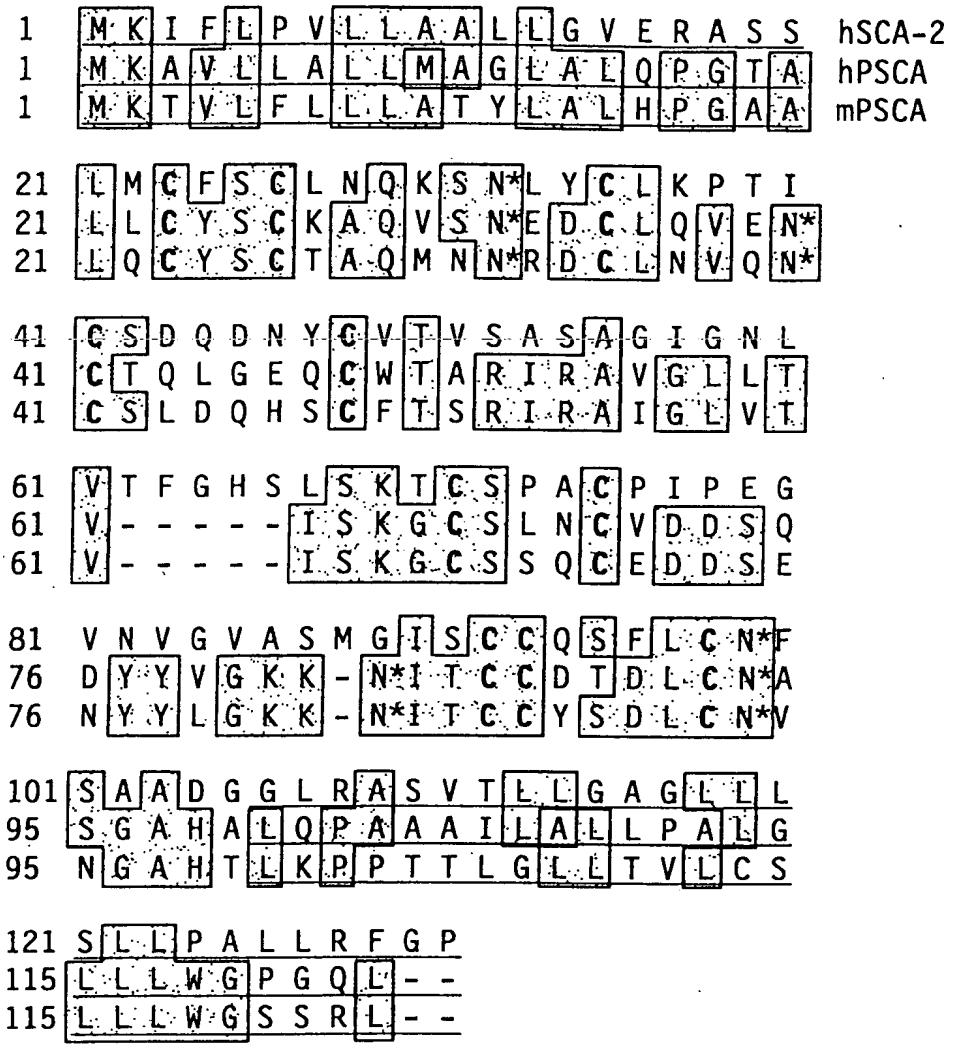
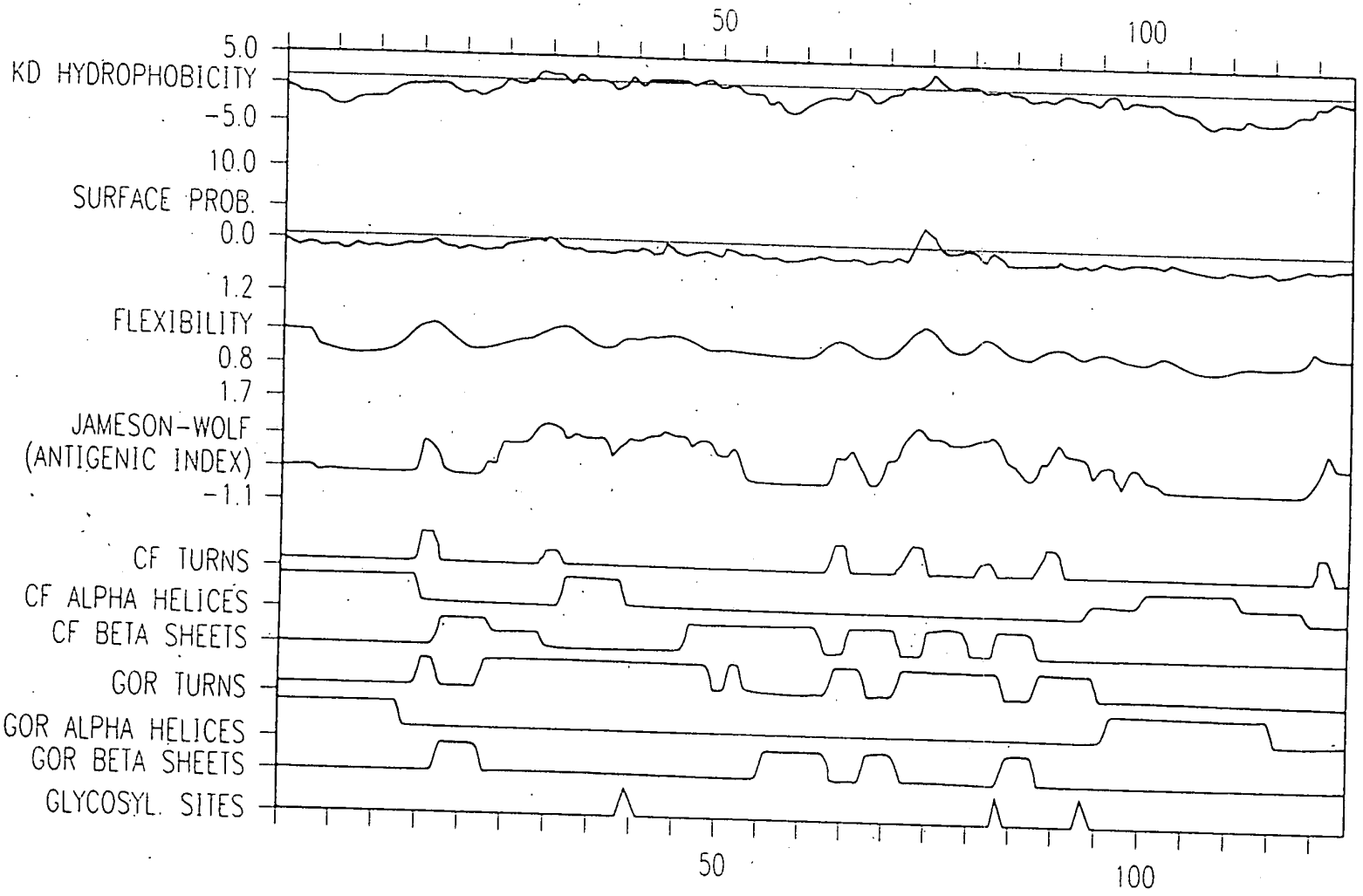


FIG. 4



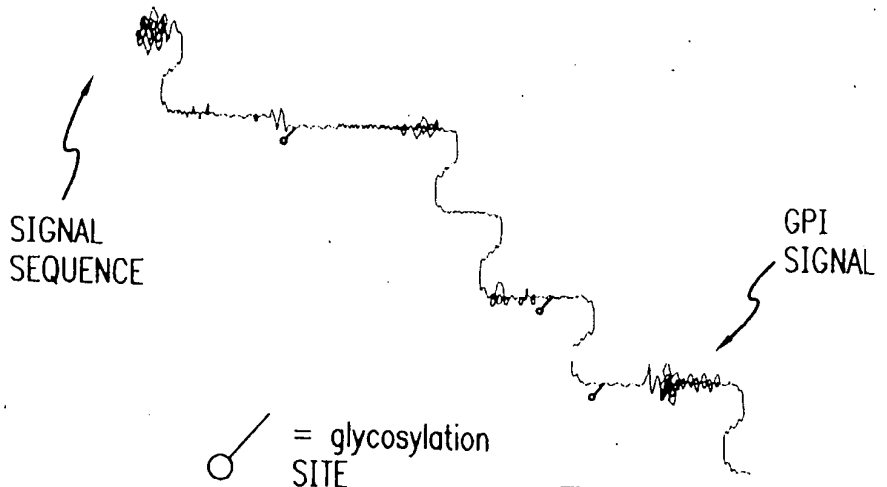
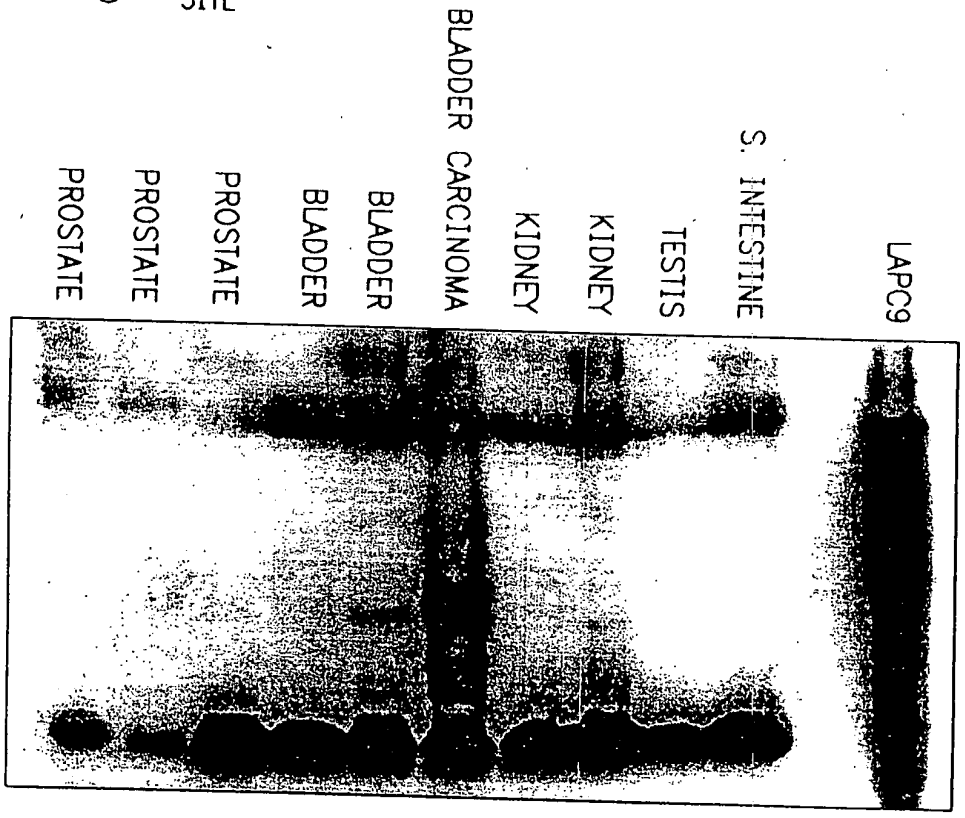


FIG. 5

FIG. 6



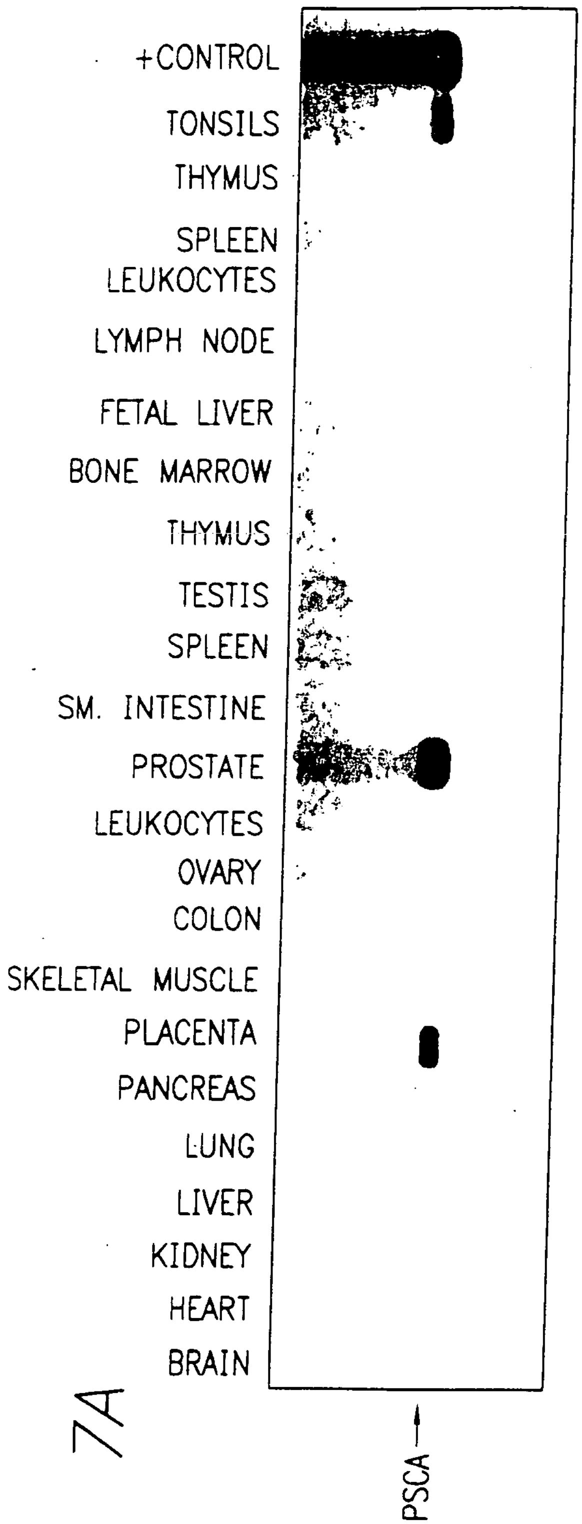

+CONTROL
TONSILS
THYMUS
SPLEEN
LEUKOCYTES
LYMPH NODE
FETAL LIVER
BONE MARROW
THYMUS
TESTIS
SPLEEN
SM. INTESTINE
PROSTATE
LEUKOCYTES
OVARY
COLON
SKELETAL MUSCLE
PLACENTA
PANCREAS
LUNG
LIVER
KIDNEY
HEART
BRAIN
PSCA

FIG. 7A

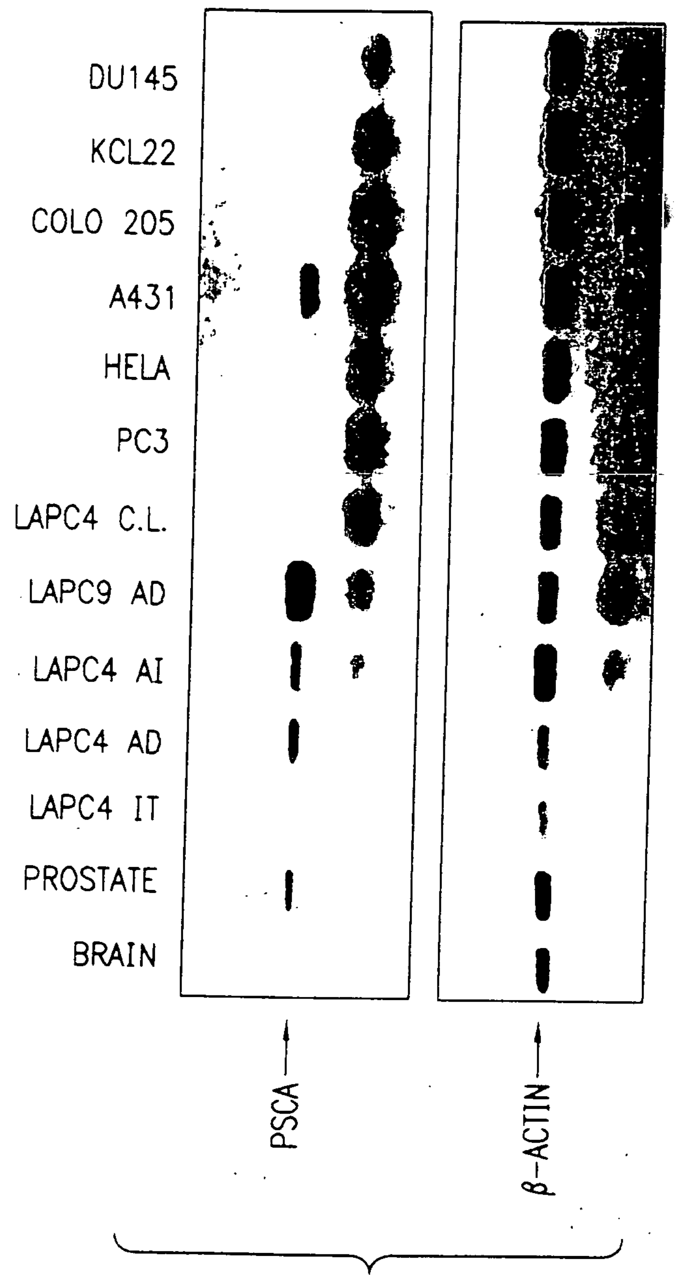

DU145
KCL22
COLO 205
A431
HELA
PC3
LAPC4 C.L.
LAPC9 AD
LAPC4 AI
LAPC4 AD
LAPC4 IT
PROSTATE
BRAIN
PSCA
β-ACTIN

FIG. 7B

FIG. 8A

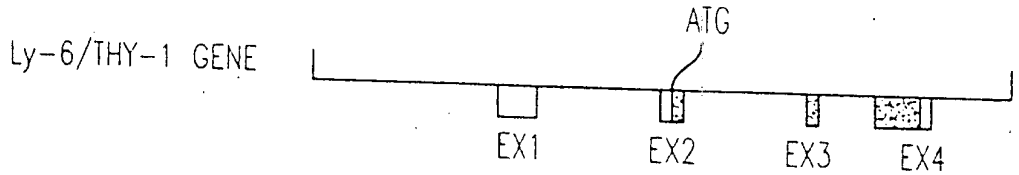


FIG. 8B

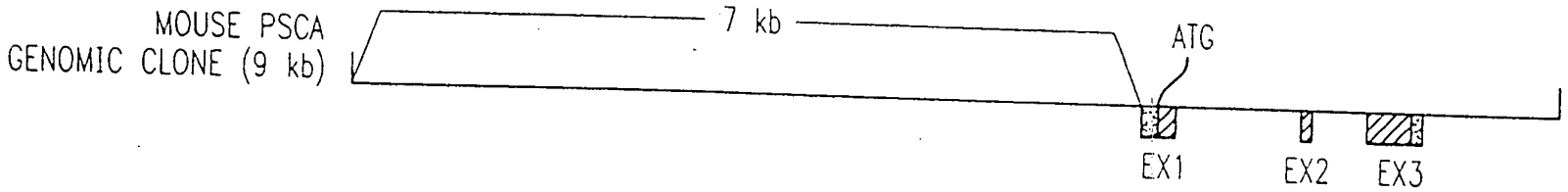
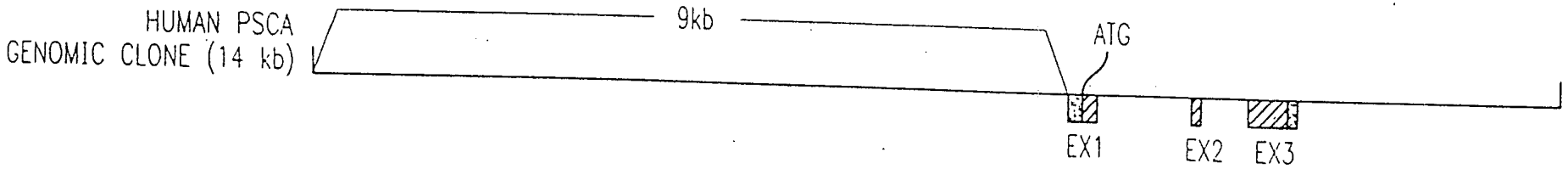


FIG. 8C



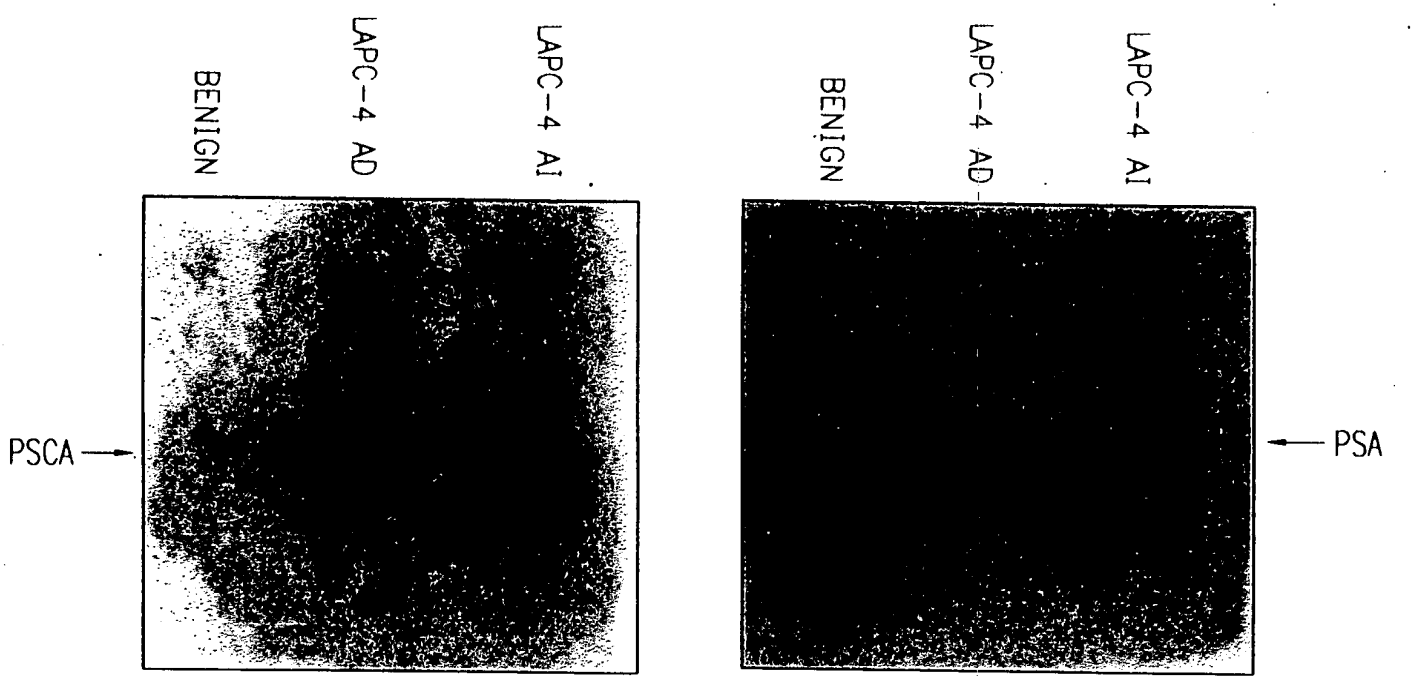


FIG. 9A

FIG. 9B

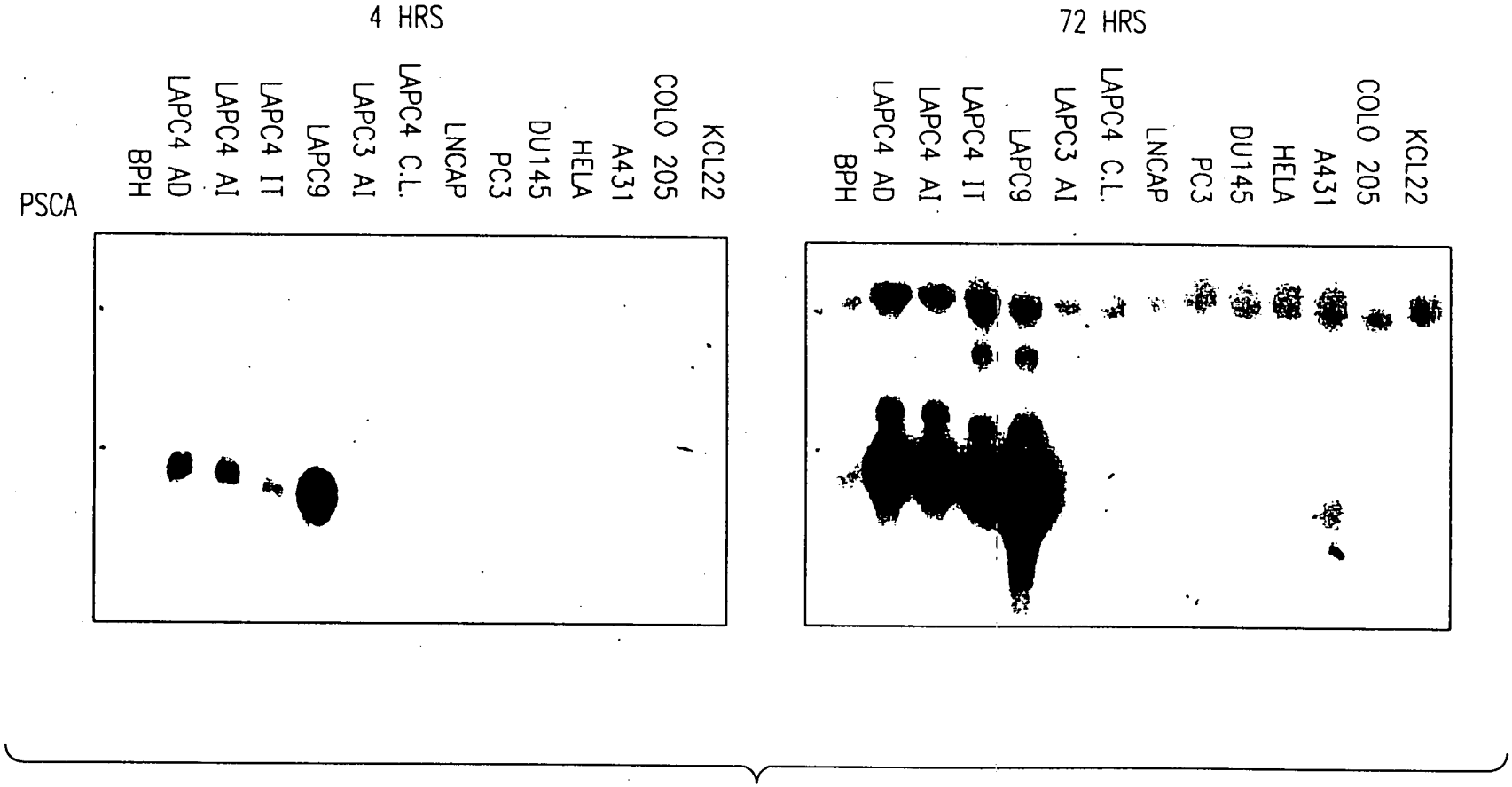


FIG. 10A

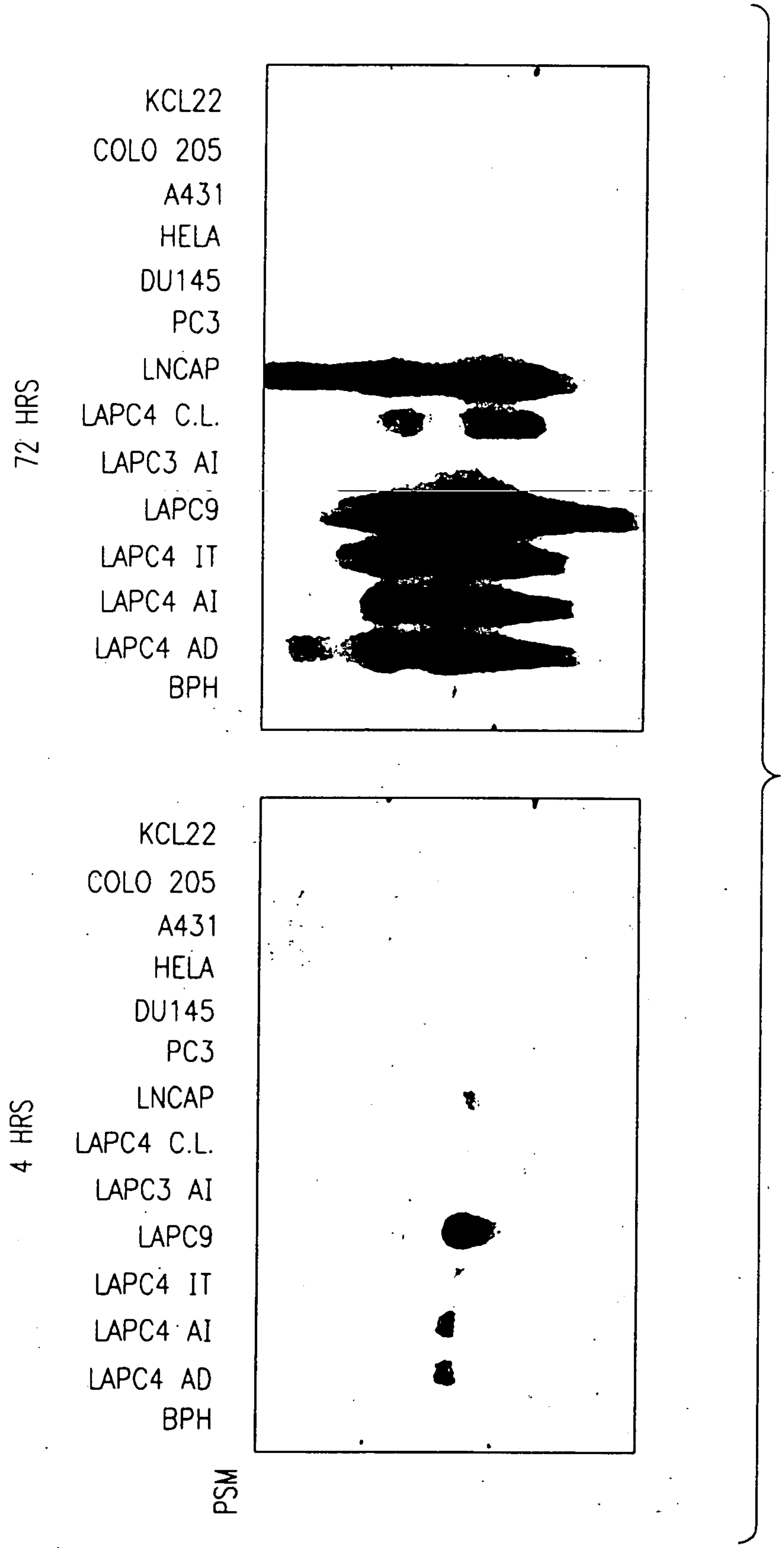

72 HRS
KCL22
COLO 205
A431
HELA
DU145
PC3
LNCAP
LAPC4 C.L.
LAPC3 AI
LAPC9
LAPC4 IT
LAPC4 AI
LAPC4 AD
BPH
4 HRS
KCL22
COLO 205
A431
HELA
DU145
PC3
LNCAP
LAPC4 C.L.
LAPC3 AI
LAPC9
LAPC4 IT
LAPC4 AI
LAPC4 AD
BPH
PSM

FIG. 10B

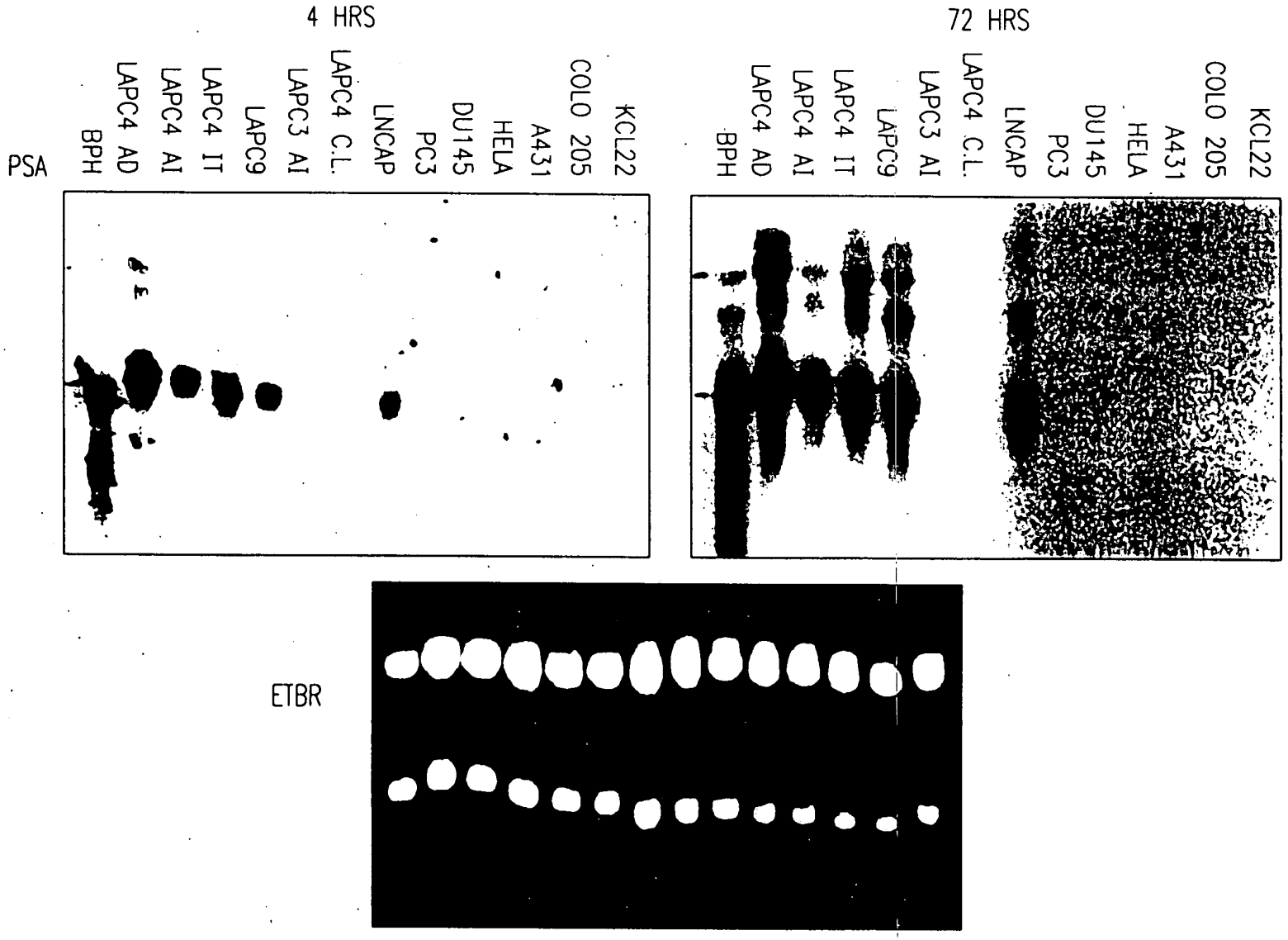


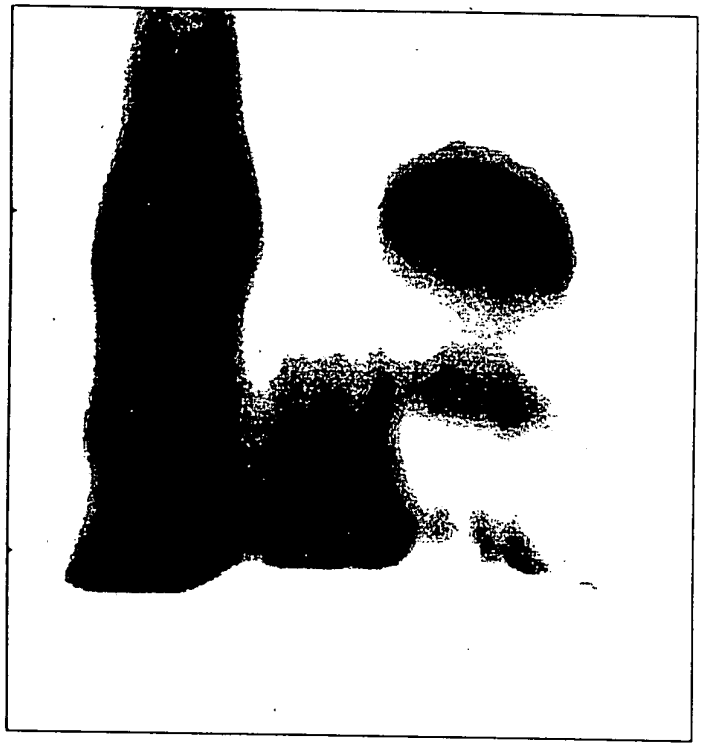
FIG. 10C

FIG. 11A

FIG. 11B

FIG. 11C

FIG. 12A



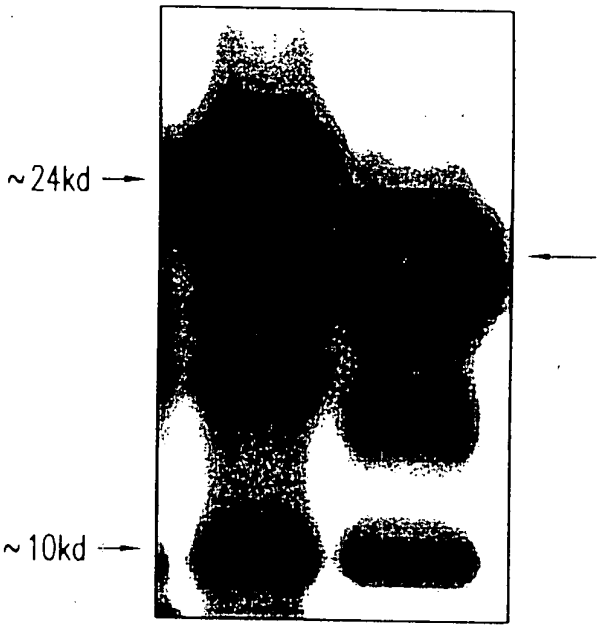


FIG. 12B

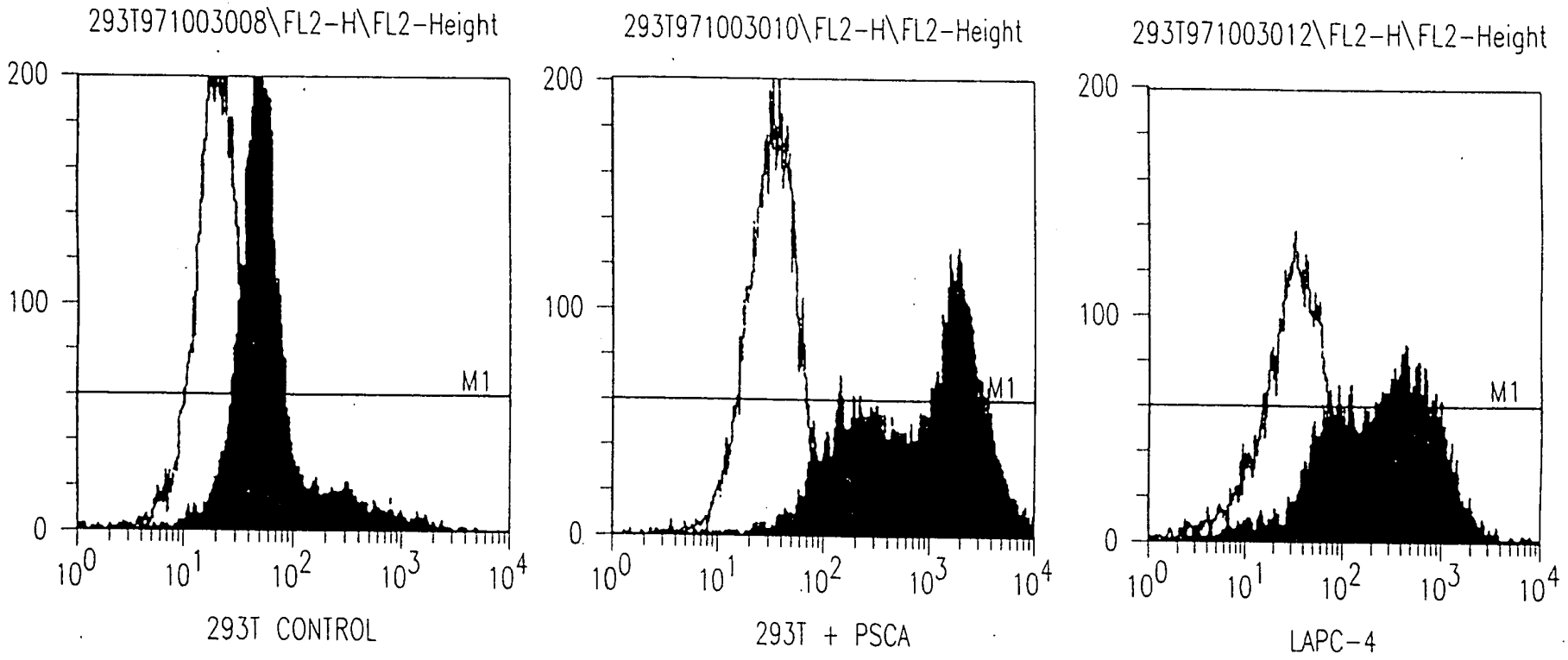

293T971003008\FL2-H\FL2-Height
200
100
0
M1
10^0 10^1 10^2 10^3 10^4
293T CONTROL
293T971003010\FL2-H\FL2-Height
200
100
0
M1
10^0 10^1 10^2 10^3 10^4
293T + PSCA
293T971003012\FL2-H\FL2-Height
200
100
0
M1
10^0 10^1 10^2 10^3 10^4
LAPC-4

FIG. 12C

FIG. 13

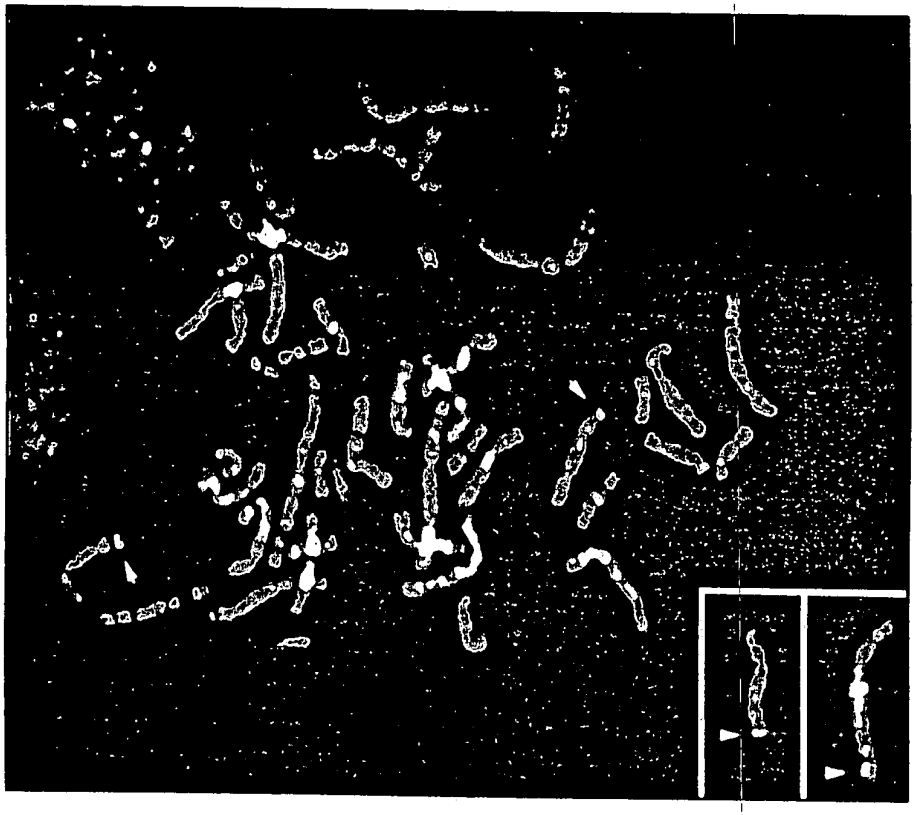


FIG. 14A

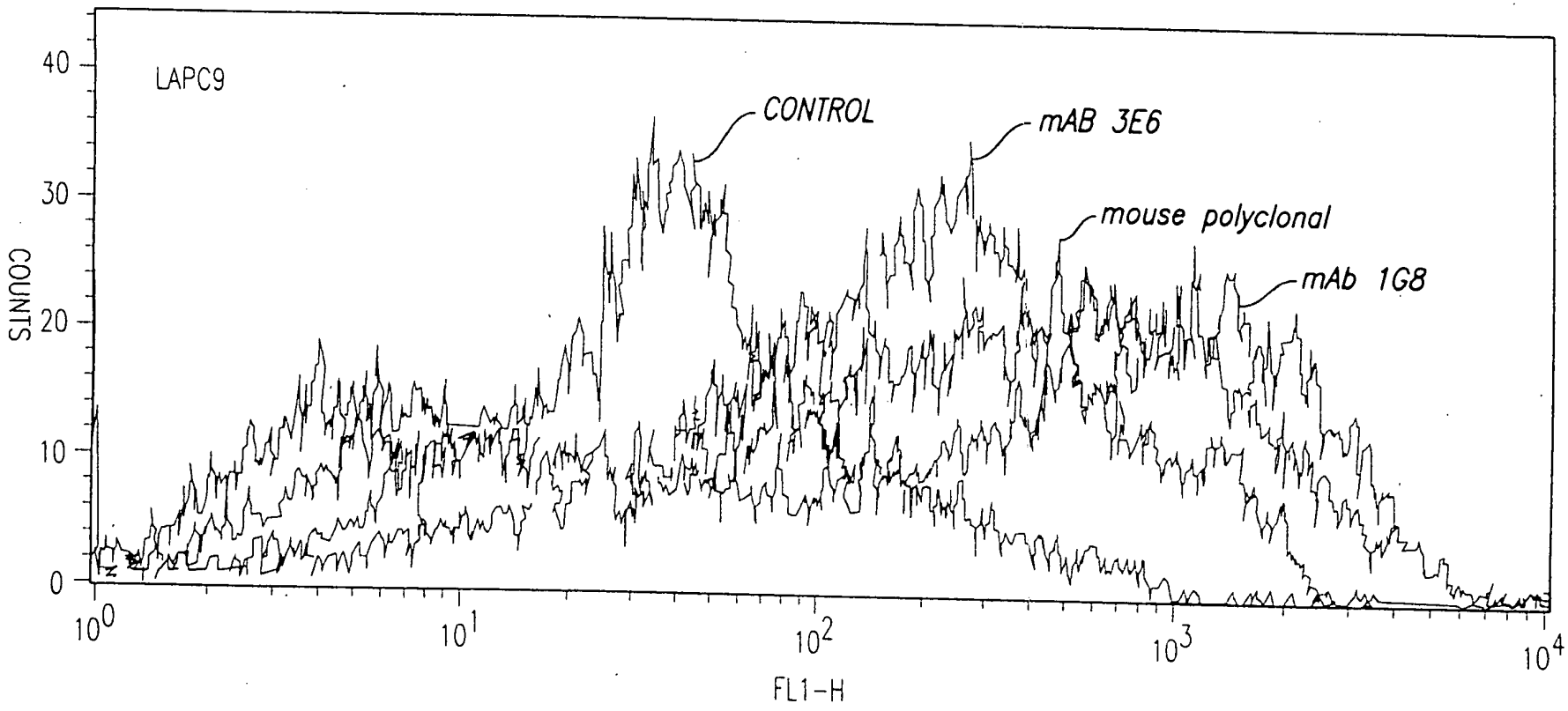


FIG. 14B

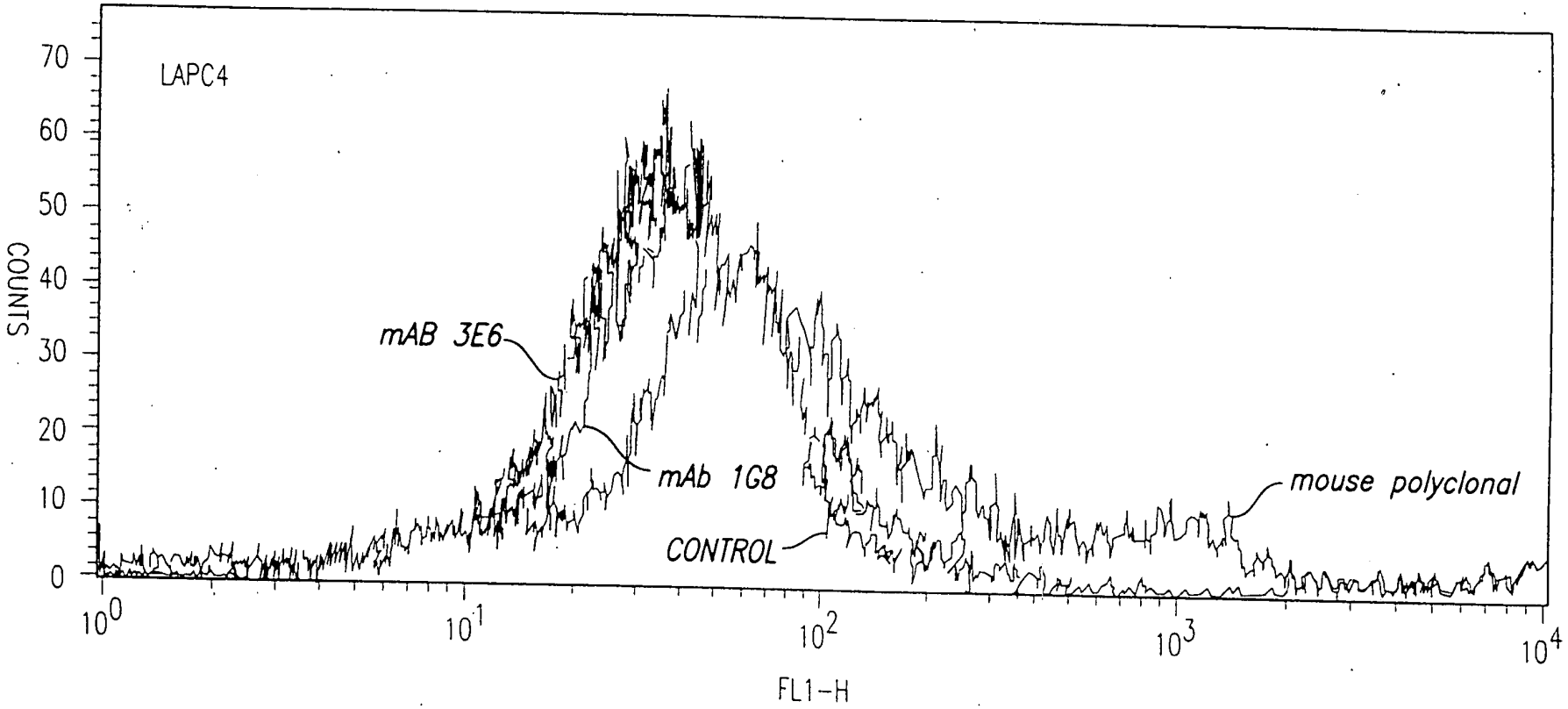
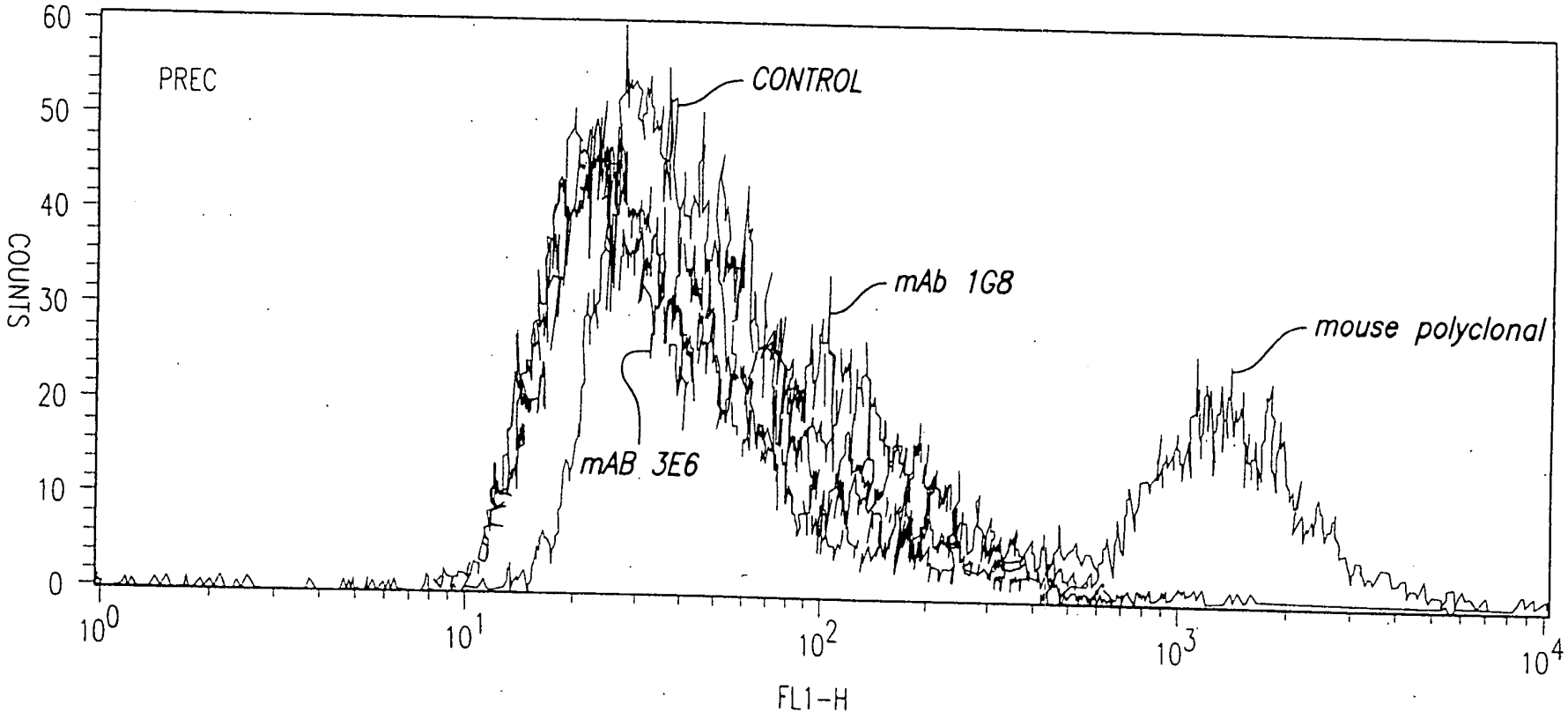

LAPC4
COUNTS
70
60
50
40
30
20
10
0
mAB 3E6
mAb 1G8
CONTROL
mouse polyclonal
10^0
10^1
10^2
10^3
10^4
FL1-H

FIG. 14C



EPITOPE MAP

mAb	ISOTYPE		FL (18–98)	N (2–50)	M (46–109)	C (85–123)
1G8	IgG1	k	2.039	0.007	0.628	0.000
2H9	IgG1	k	1.318	0.863	0.032	0.021
3C5	IgG2a	k	2.893	1.965	0.016	0.005
3E6	IgG3	k	0.328	0.024	0.069	0.370
4A10	IgG2a	k	2.039	1.315	0.000	0.014
2A2	IgG2a	k	1.366	0.733	0.010	0.003
3G3	IgG2a	k	2.805	1.731	0.004	0.000

FIG. 15A

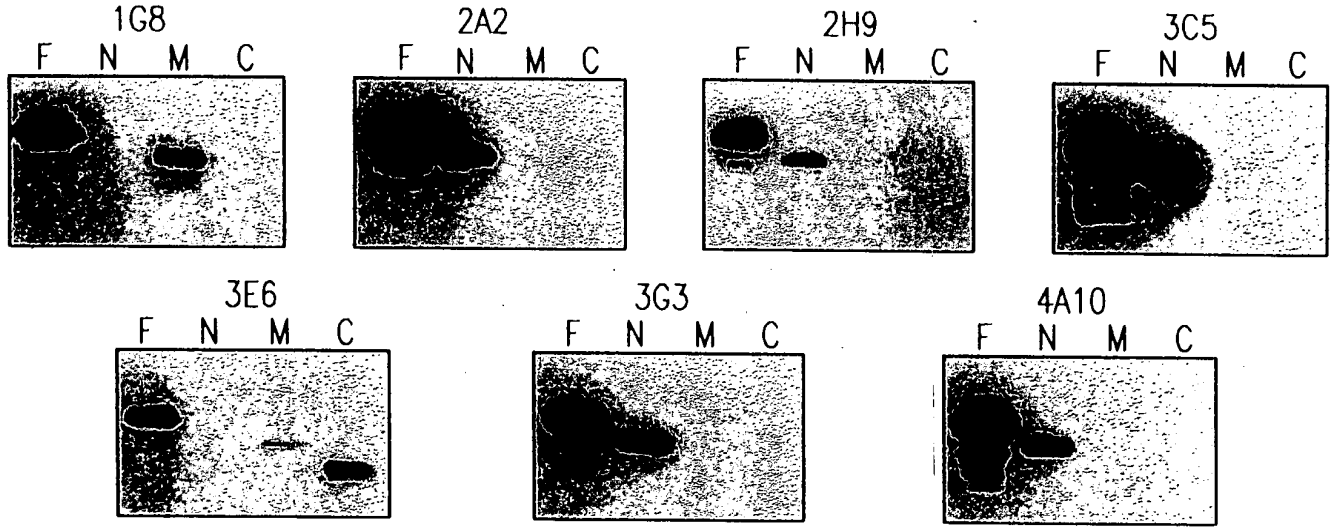
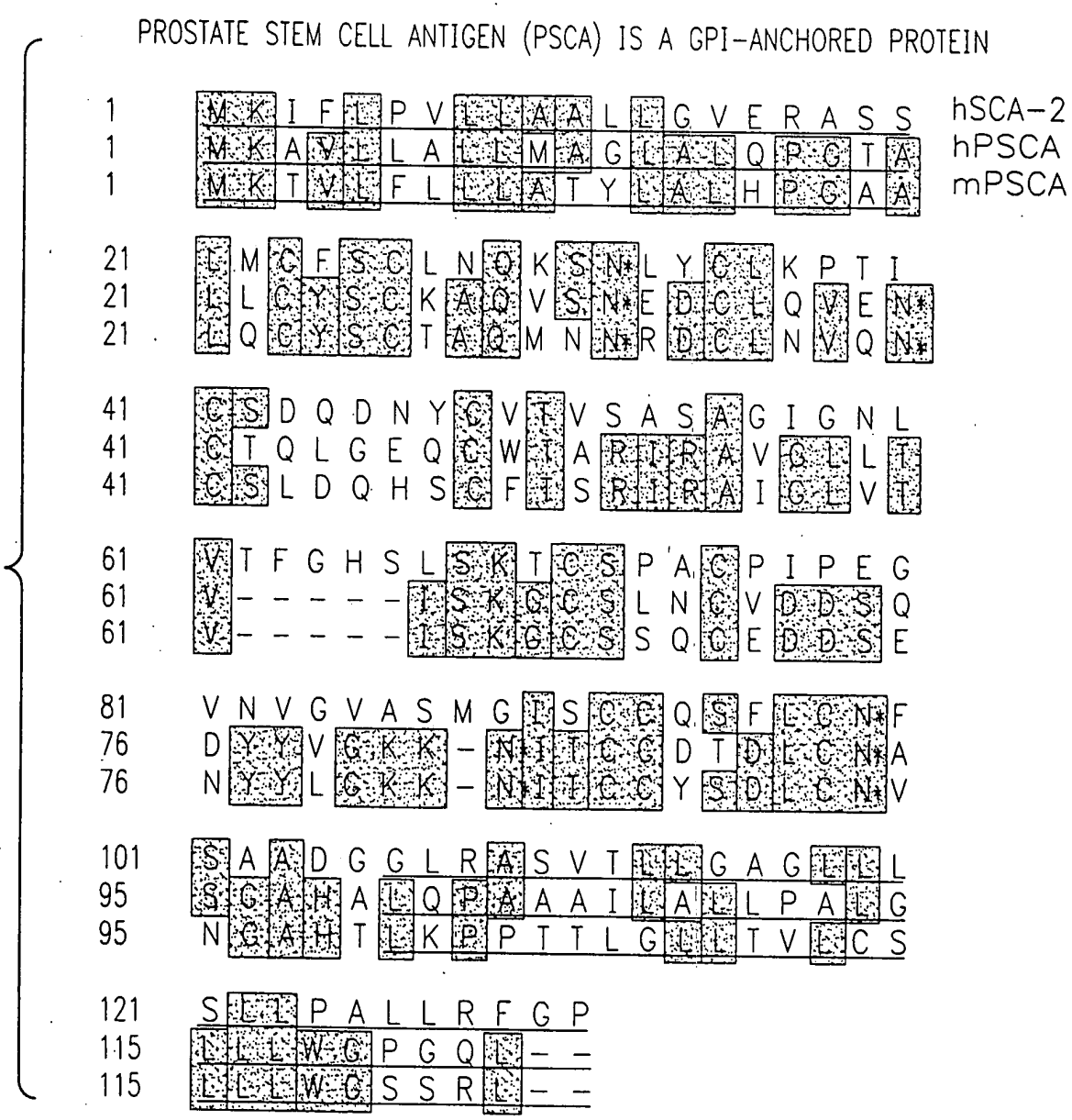


FIG. 15B

FIG. 16A



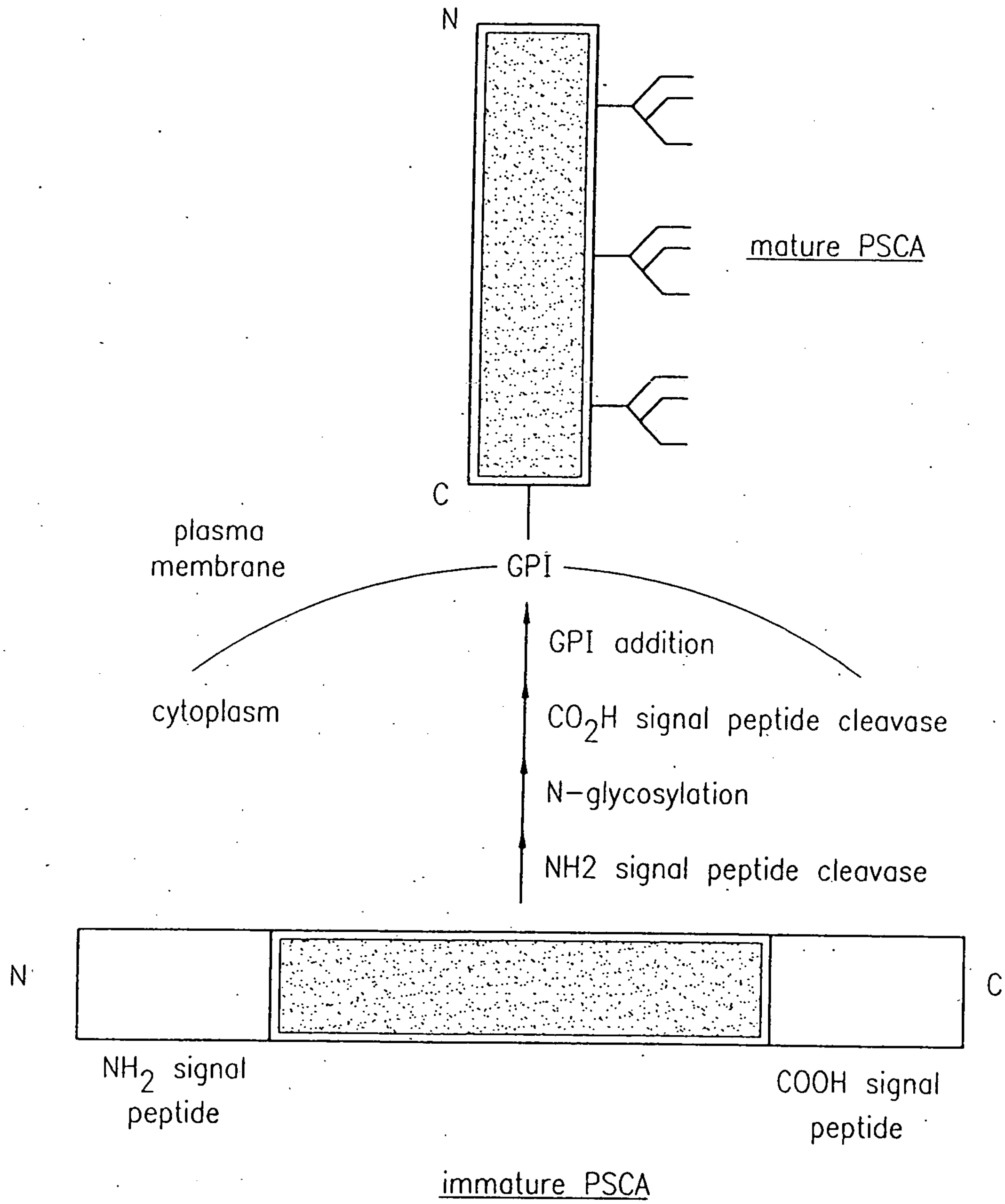


FIG. 16B

FIG. 17

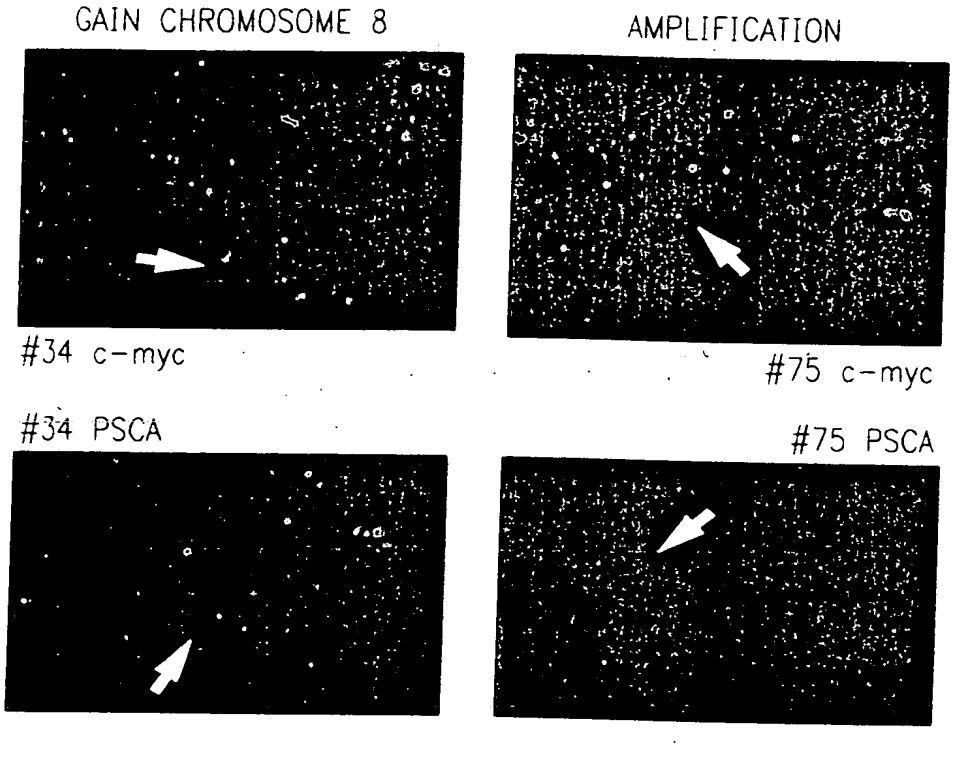
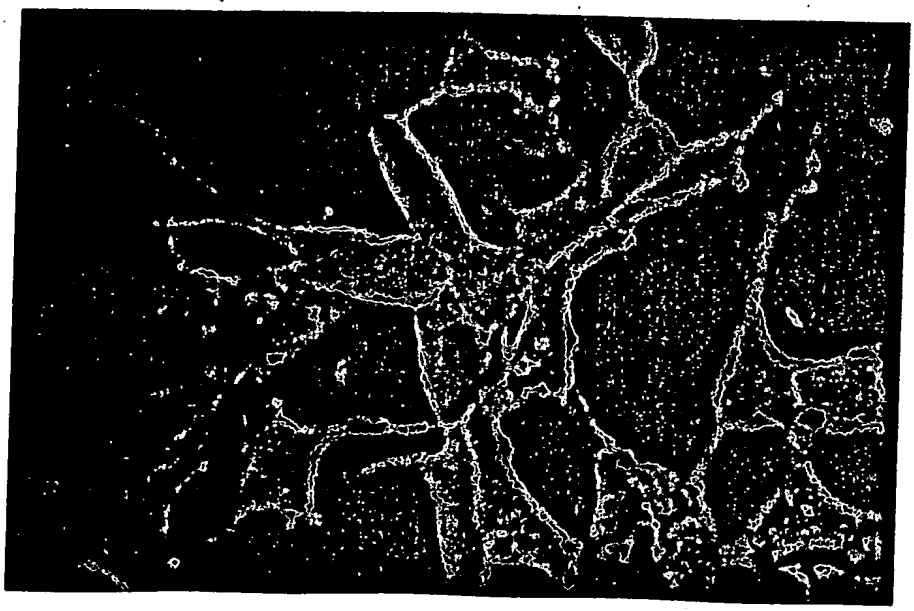


FIG. 18



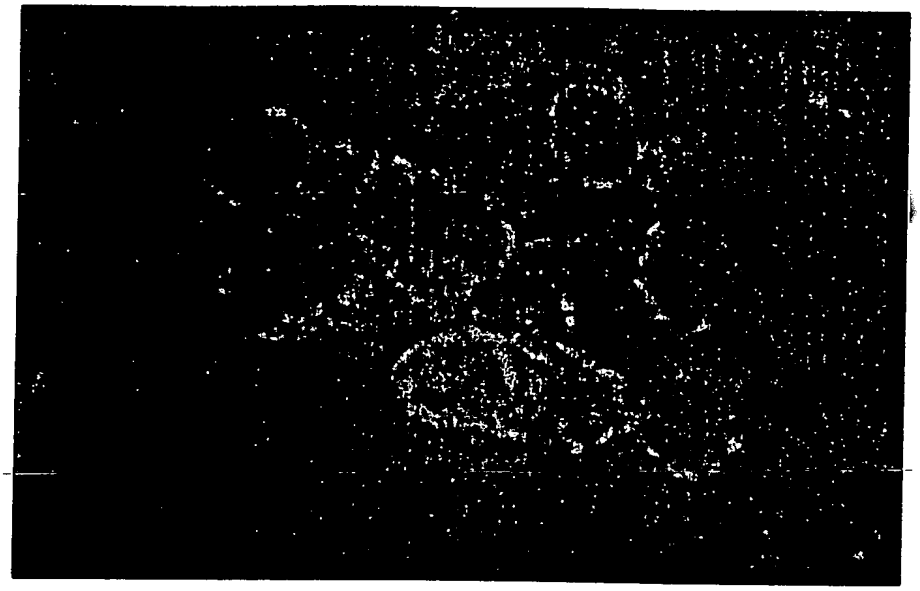


FIG. 19

FIG. 20

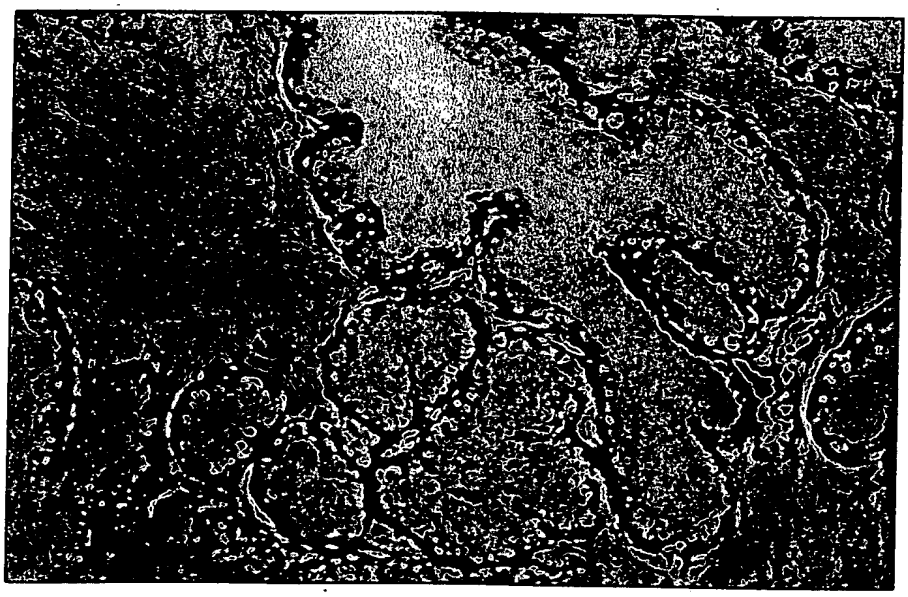


FIG. 21

PSCA IMMUNOSTAINING OF PRIMARY TUMORS

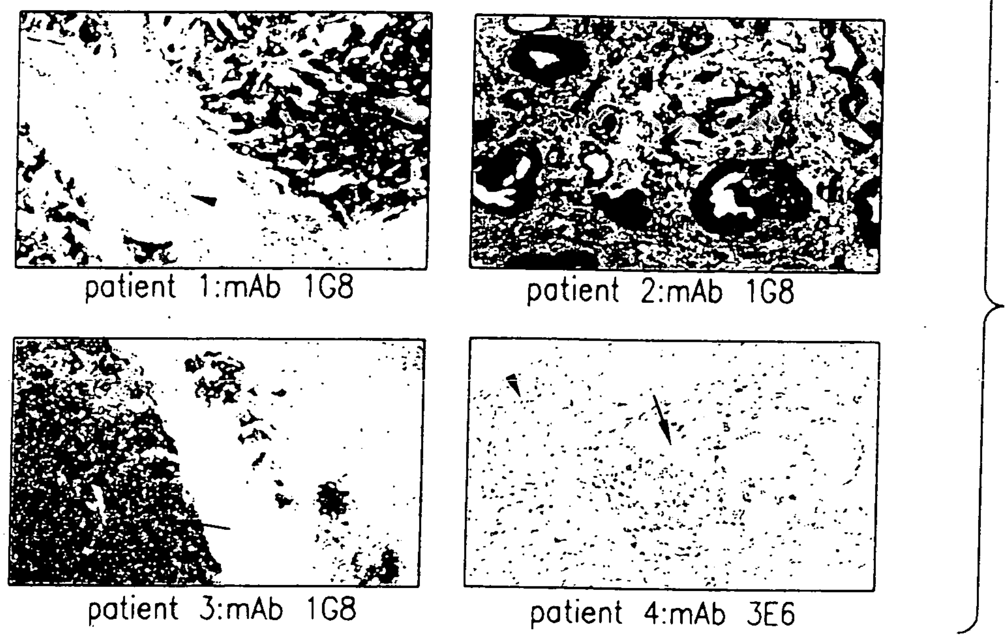
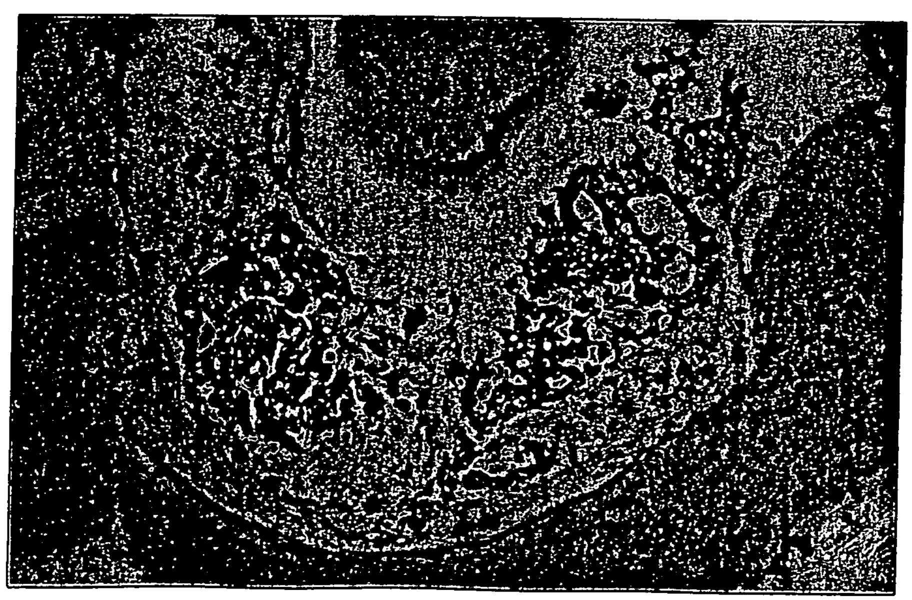


FIG. 22



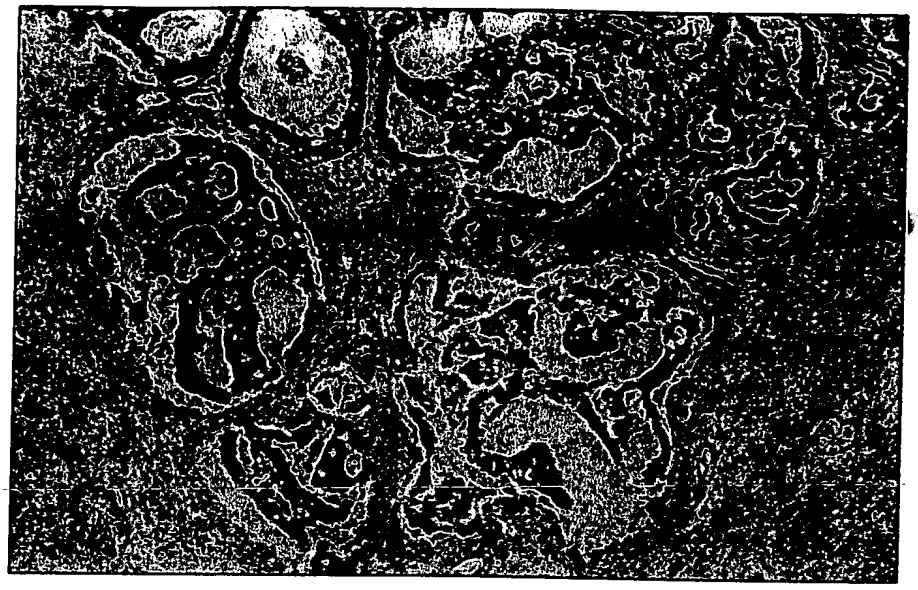
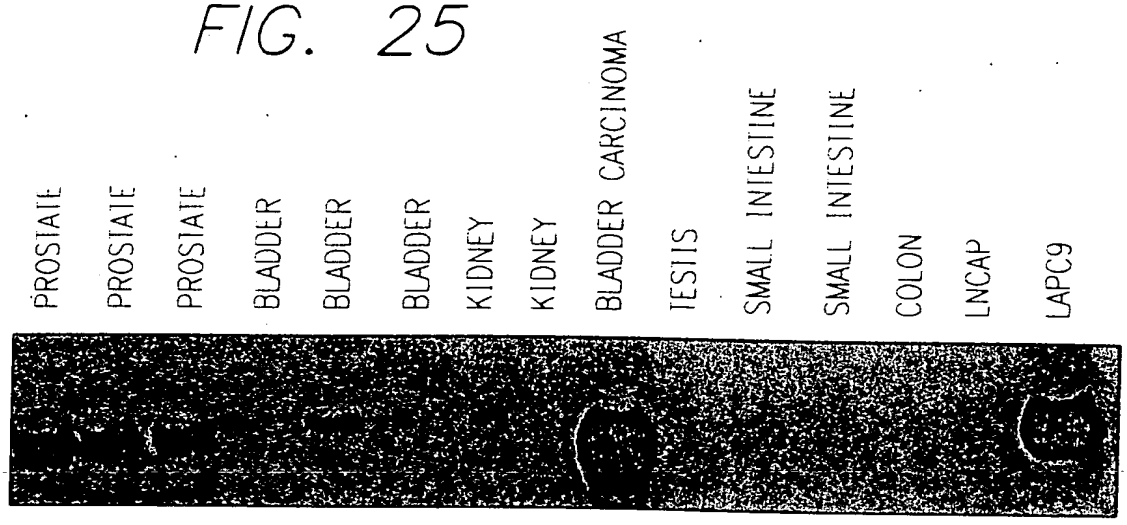


FIG. 23

FIG. 24

FIG. 25



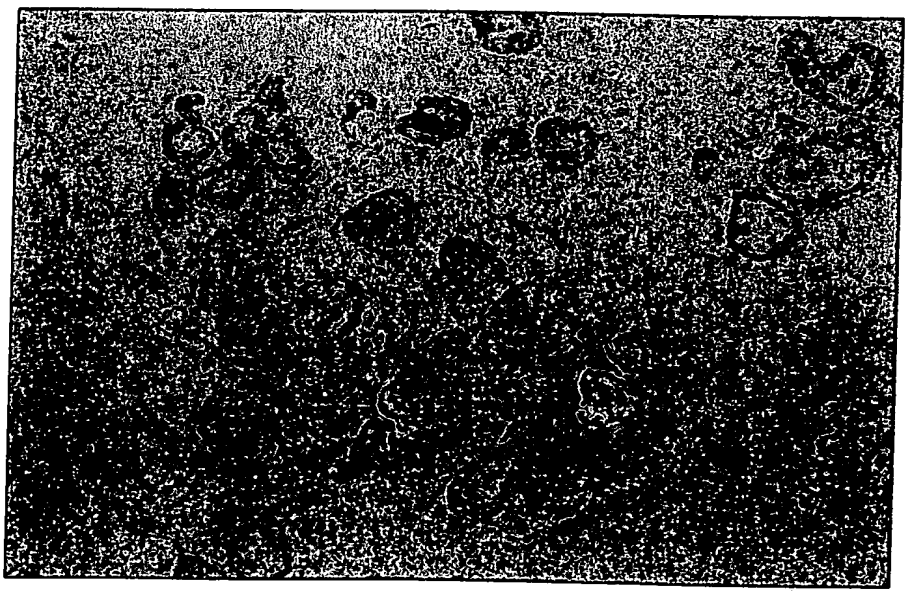


FIG. 26

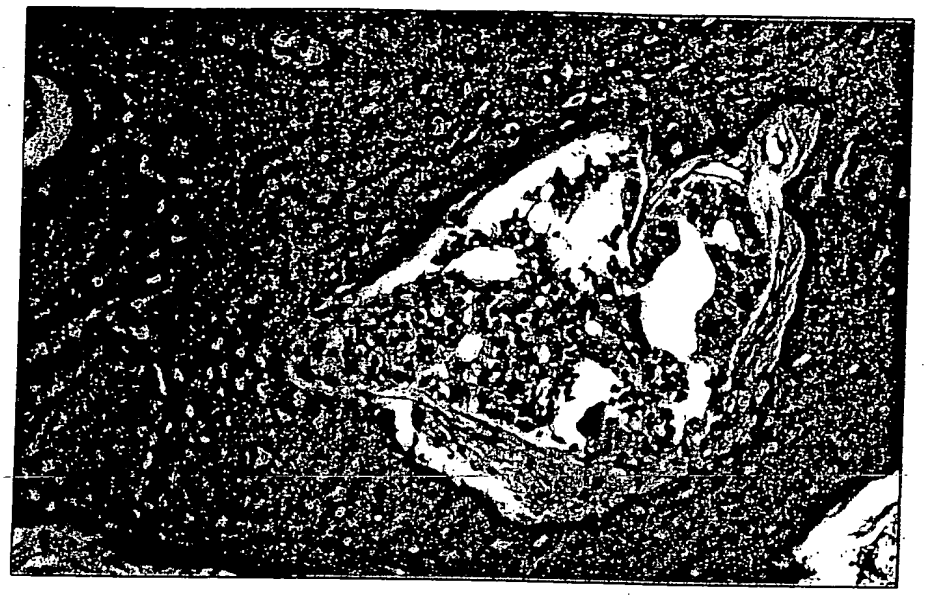
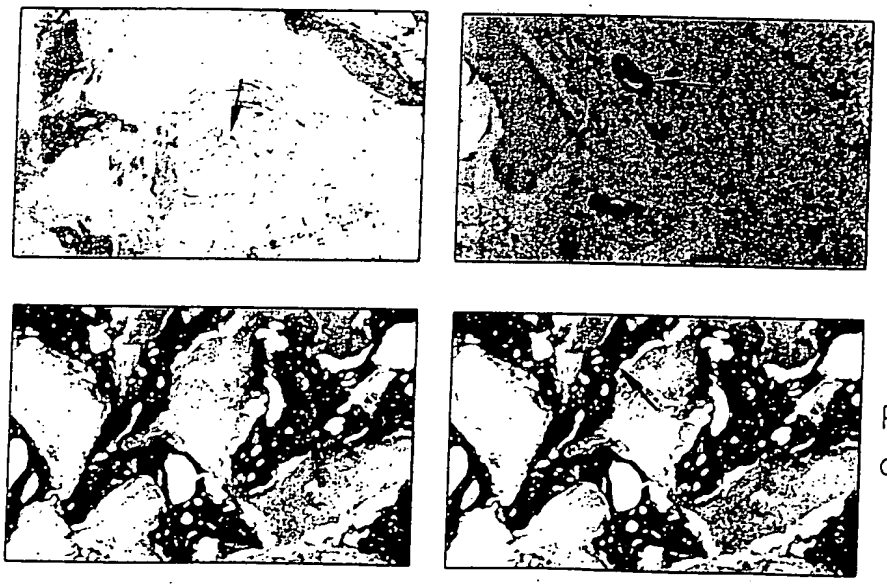


FIG. 27



Patient 5: H and E and mAb 1G8

Patient 4: H and E and mAb 3E6

FIG. 28

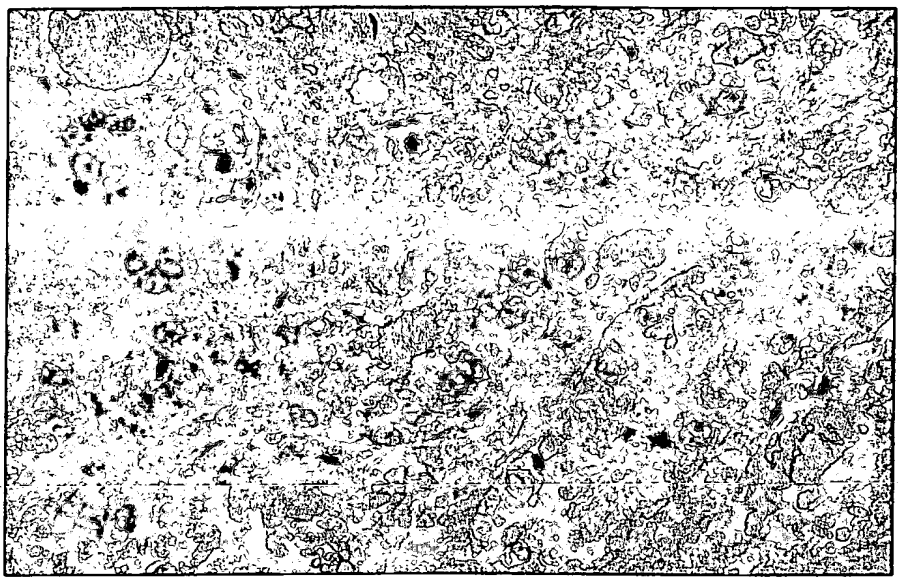


FIG. 29

FIG. 30

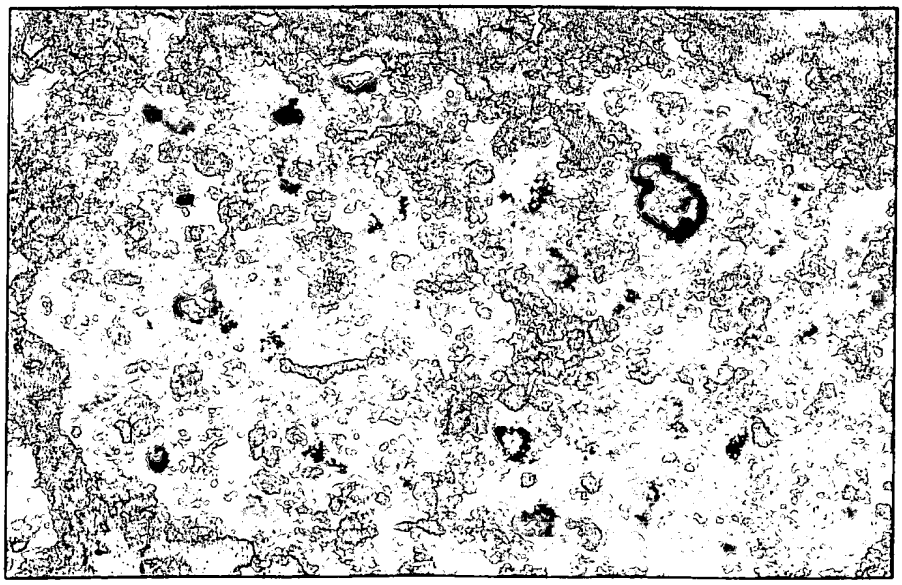
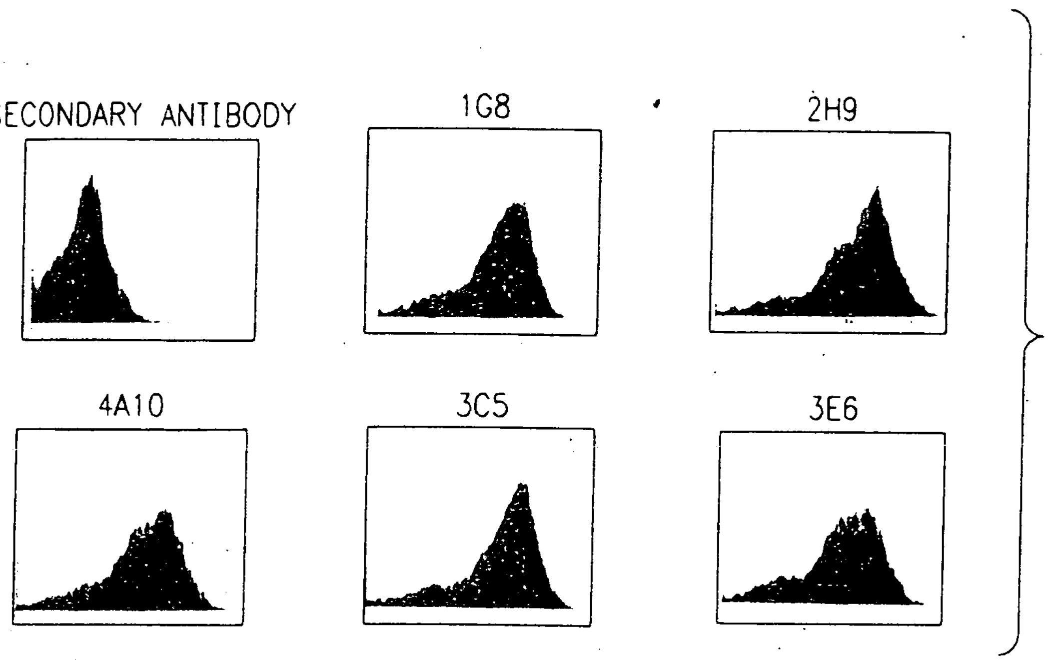


FIG. 31

FIG. 32

FIG. 33



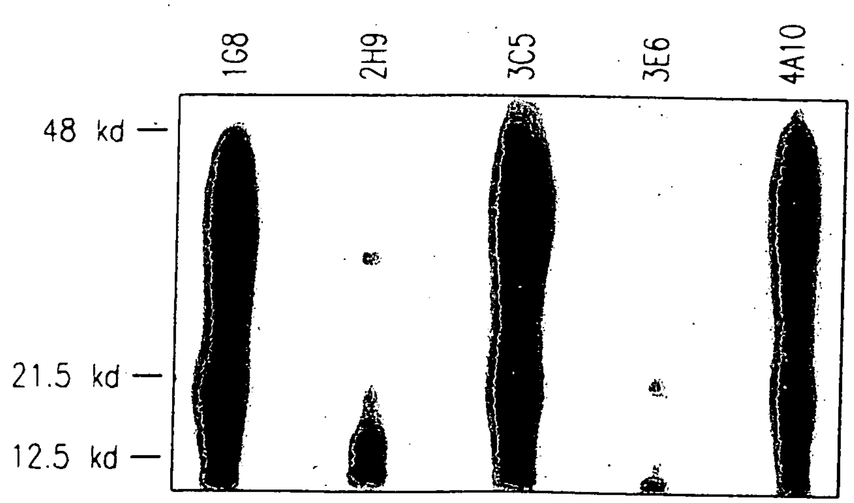
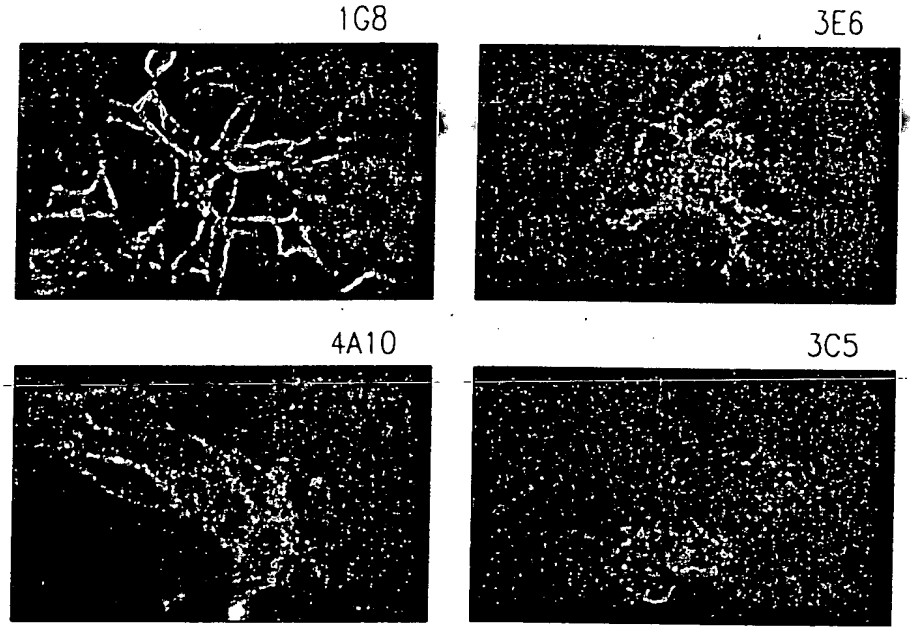


FIG. 34

FIG. 35



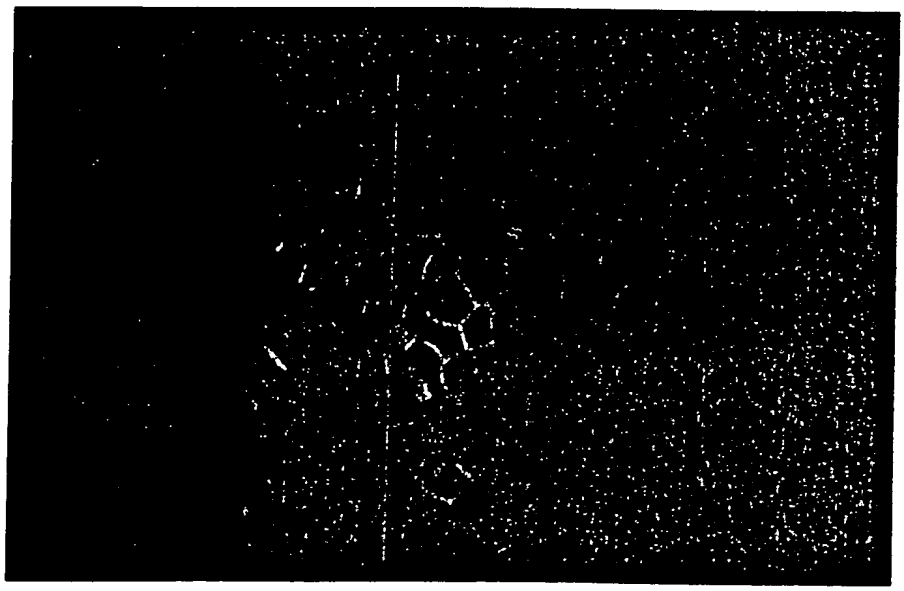


FIG. 36

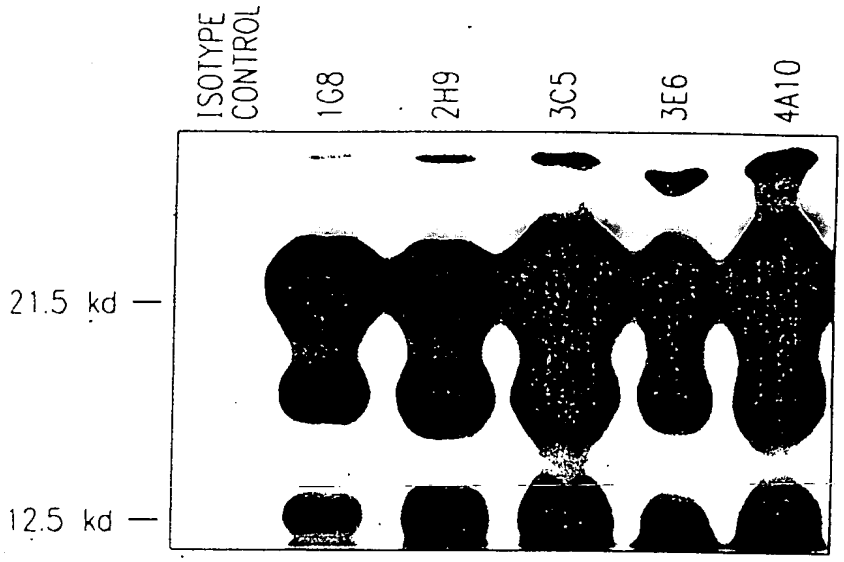


FIG. 37

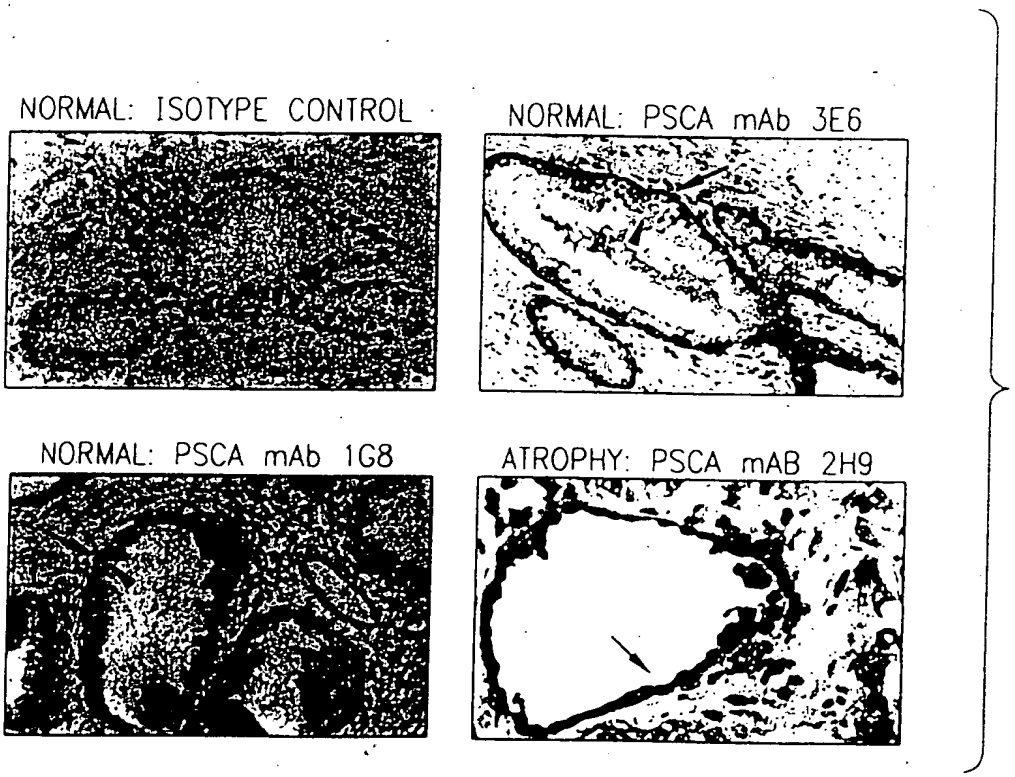
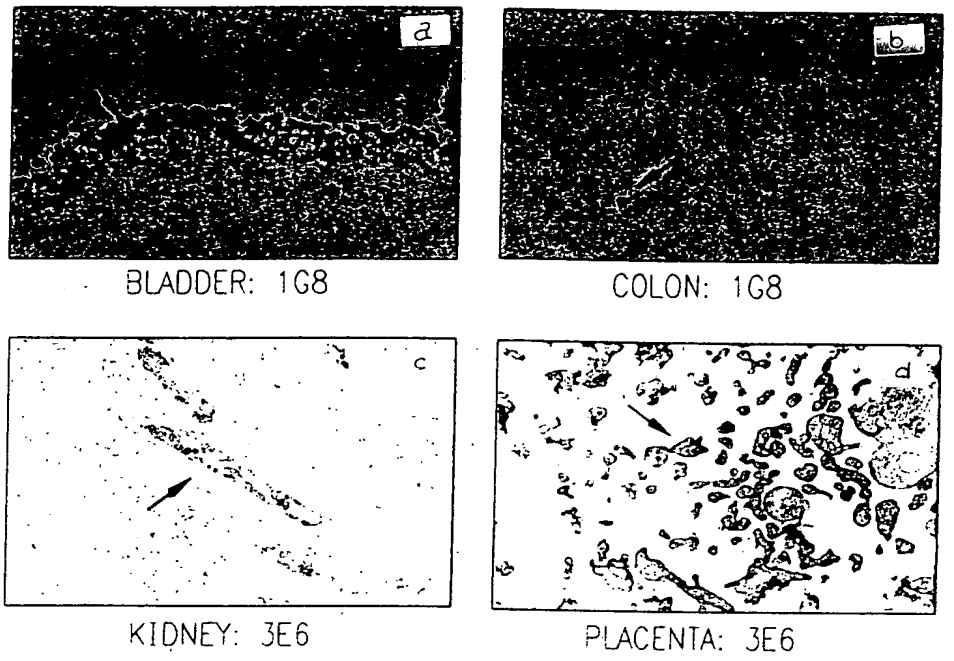


FIG. 38

FIG. 39A



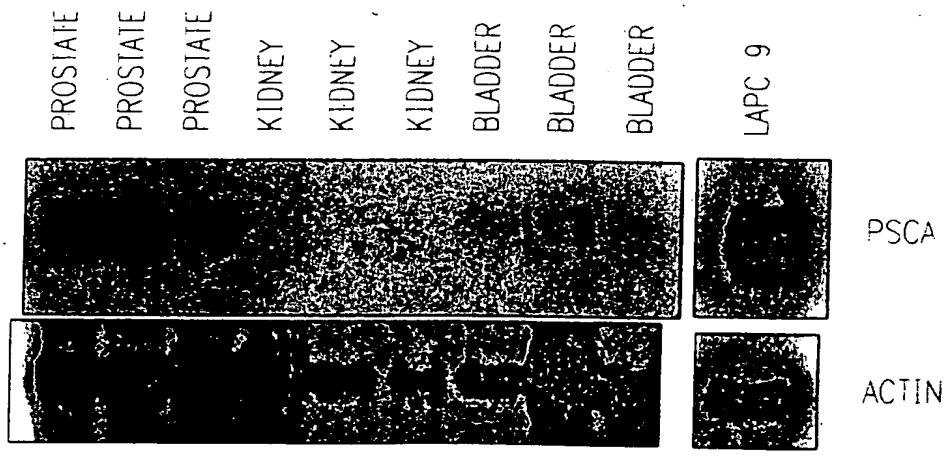
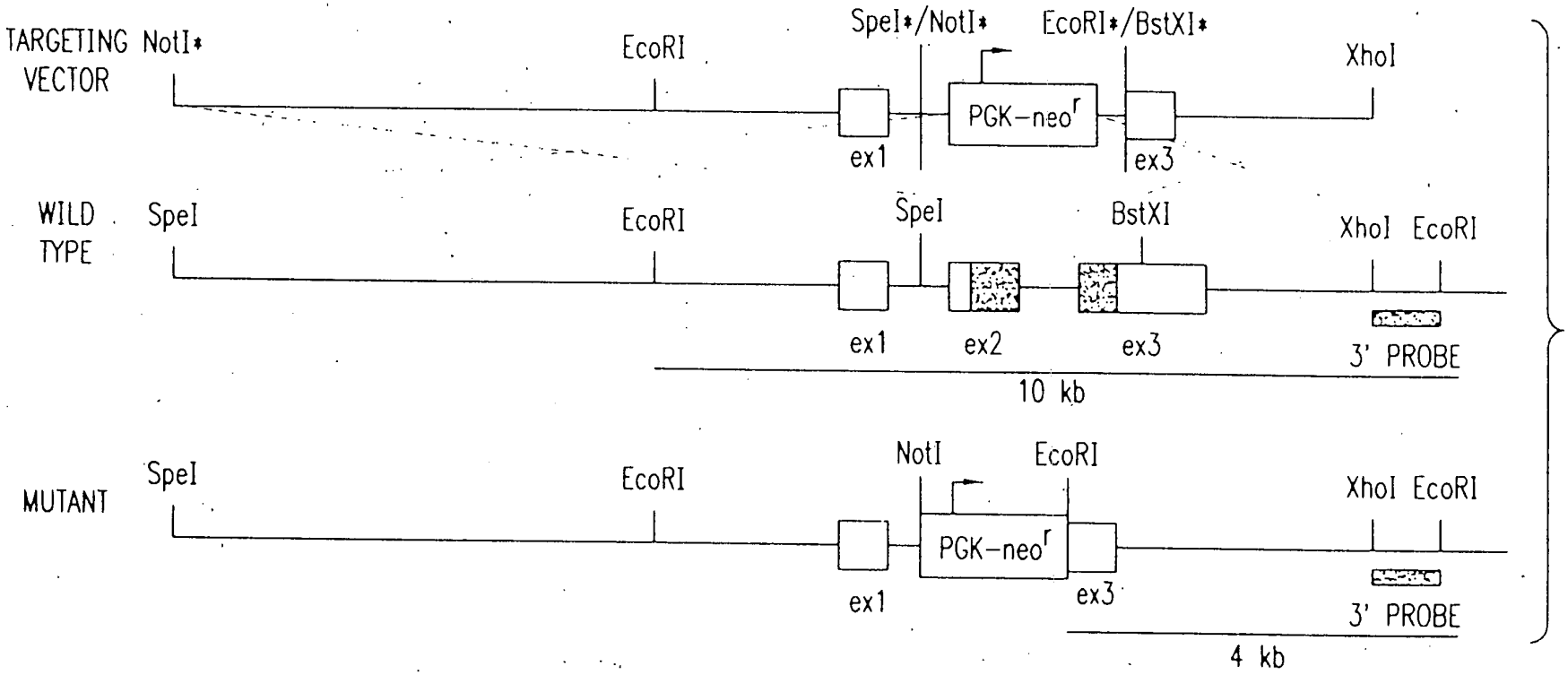


FIG. 39B

FIG. 40A



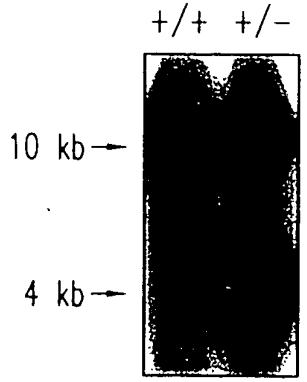


FIG. 40B

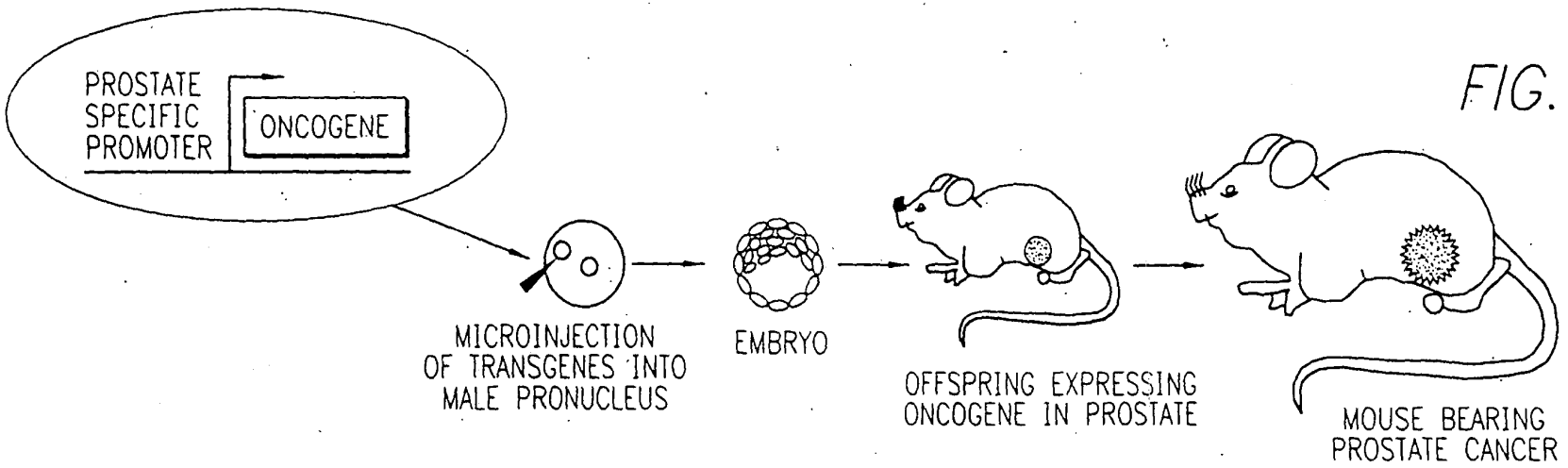


FIG. 41

TRANSGENE	TARGET TISSUES	CHARACTERISTICS
C3(1) (-3 kb)/ SV40 LARGE+SMALL, T MAROULAKOU et al. 1994 PNAS	PROSTATE (SECRETORY CELLS) URETHRAL, MAMMARY AND SWEAT GLAND	LOW-GRADE PIN 8-12 WKS HIGH-GRADE PIN 8-12 WKS INVASIVE CARCICINOMA 28 WKS NO METASTASES
PROBASIN (-426 bp)/ SV40 LARGE+SMALL, T GREENBERG et al. 1995 PNAS	PROSTATE (SECRETORY CELLS)	LOW-GRADE PIN 5-8 WKS HIGH-GRADE PIN 8-12 WKS INVASIVE CARCICINOMA 12 WKS METASTASES IN LYMPH NODE, LUNG, LIVER AND BONE
CRYPTDIN2 (-6.5 kb)/ SV40 LARGE+SMALL, T GARABEDIAN et al. 1998 PNAS	PROSTATE (NEUROENDOCRINE CELLS) SMALL INTESTINE	LOW-GRADE PIN 8-12 WKS HIGH-GRADE PIN 8-12 WKS INVASIVE CARCICINOMA 16 WKS METASTASES IN LYMPH NODE, LUNG, LIVER, AND BONE

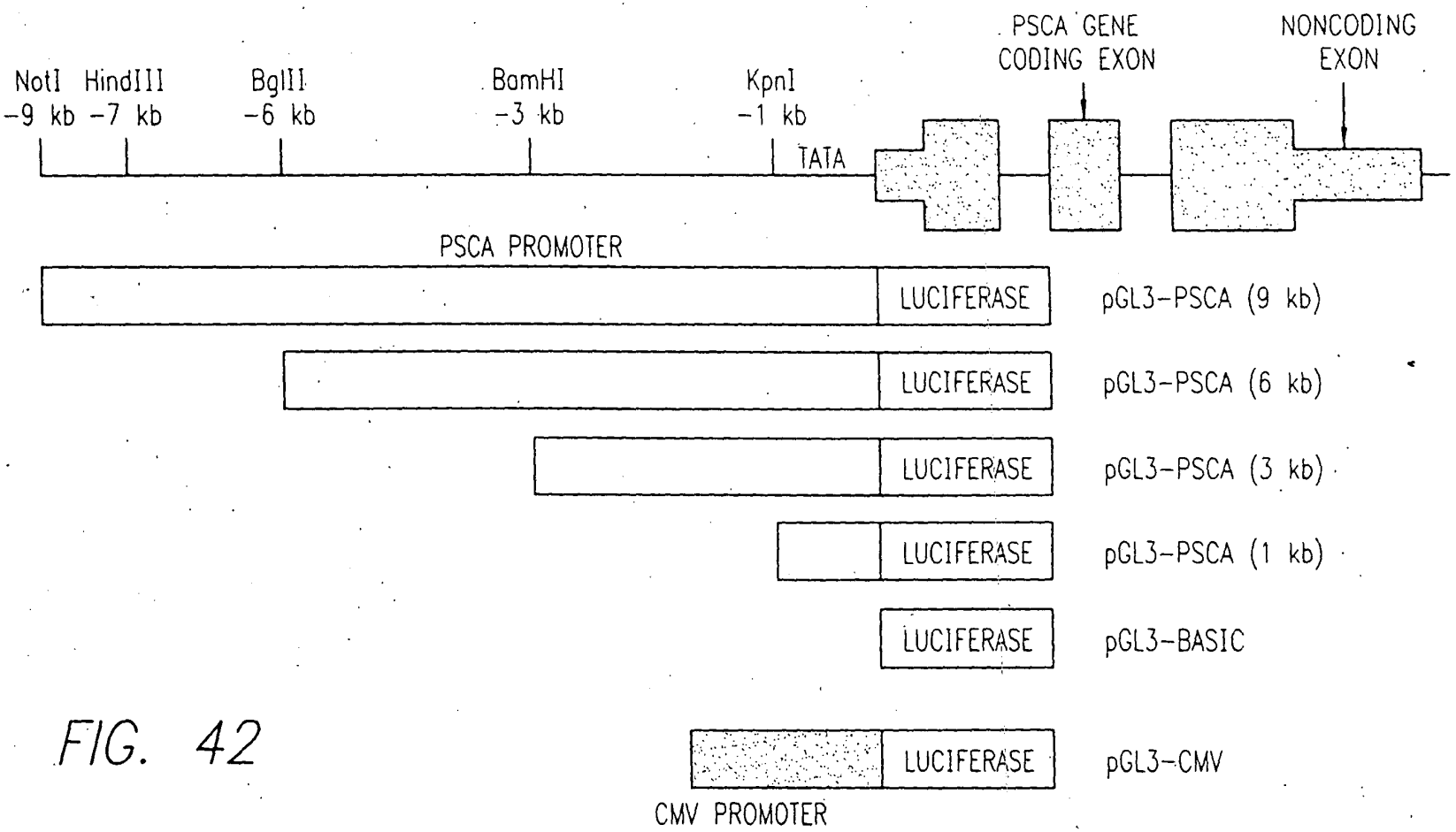


FIG. 42

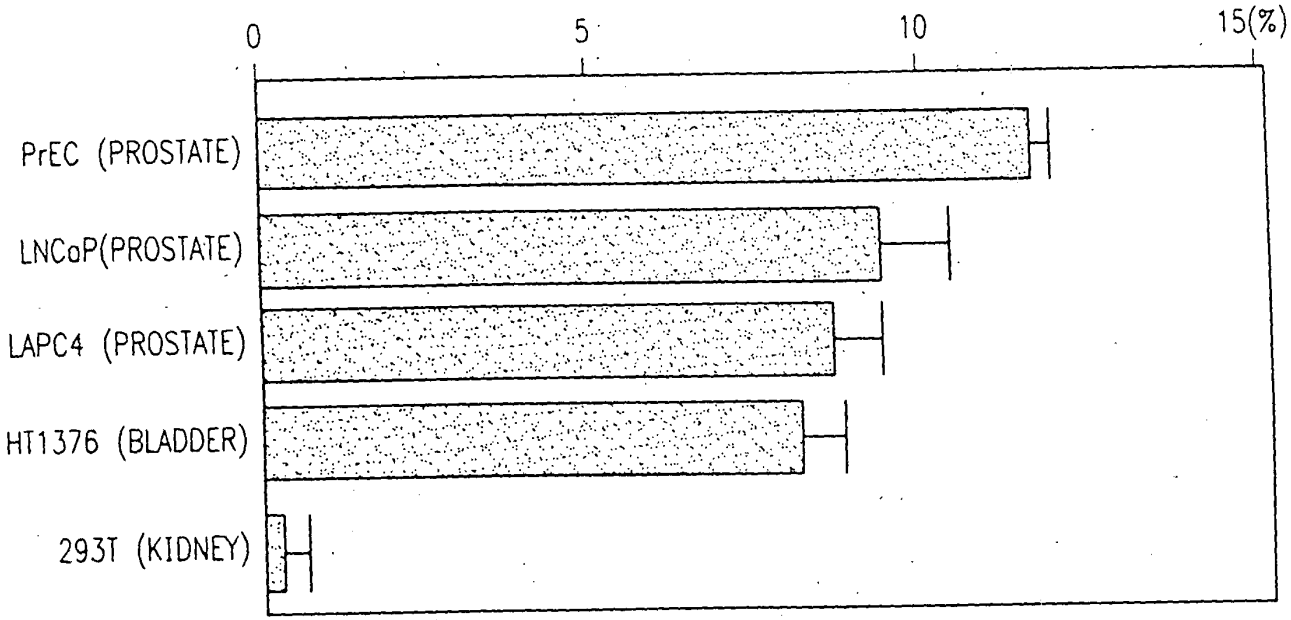


FIG. 43

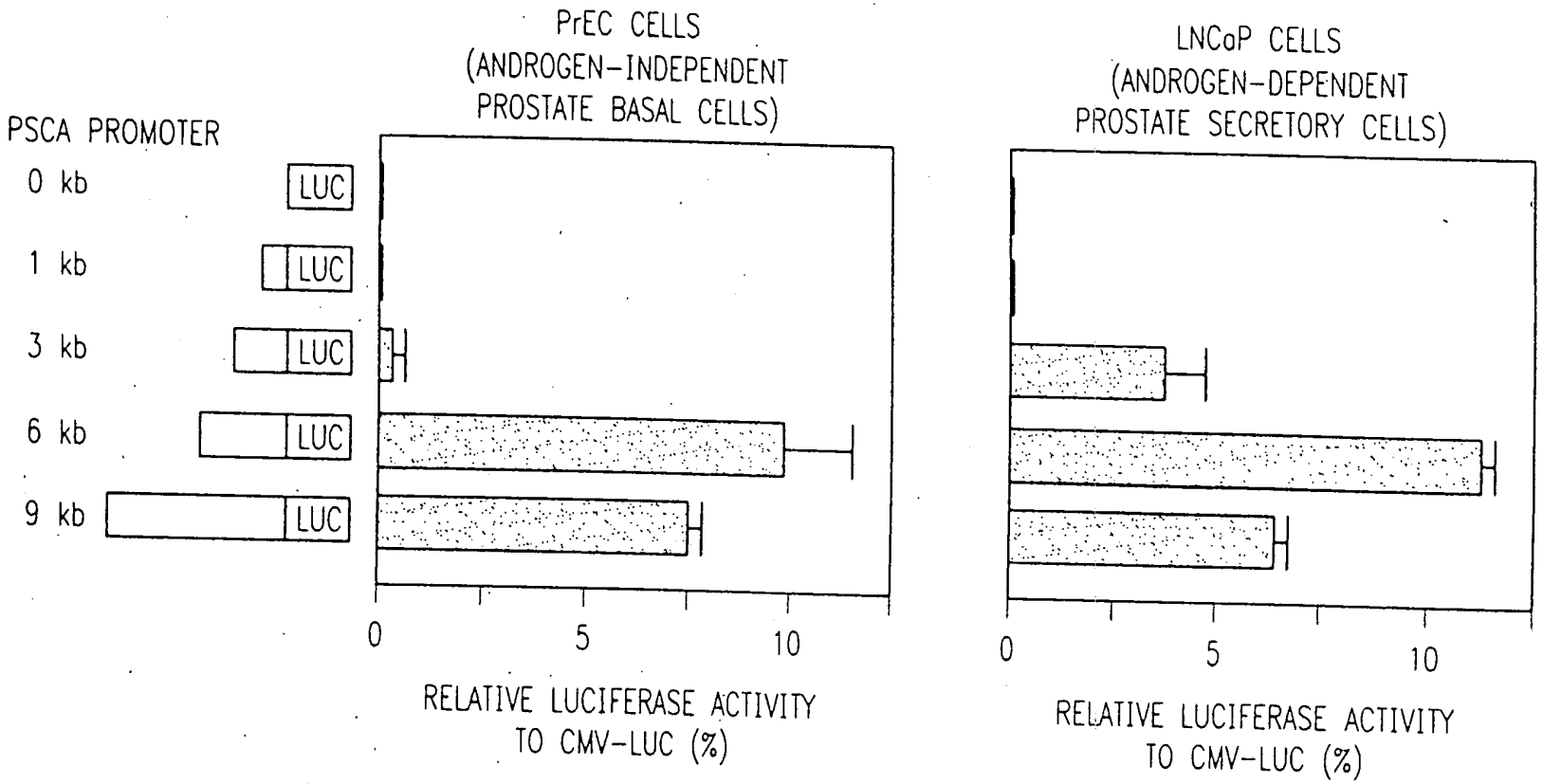
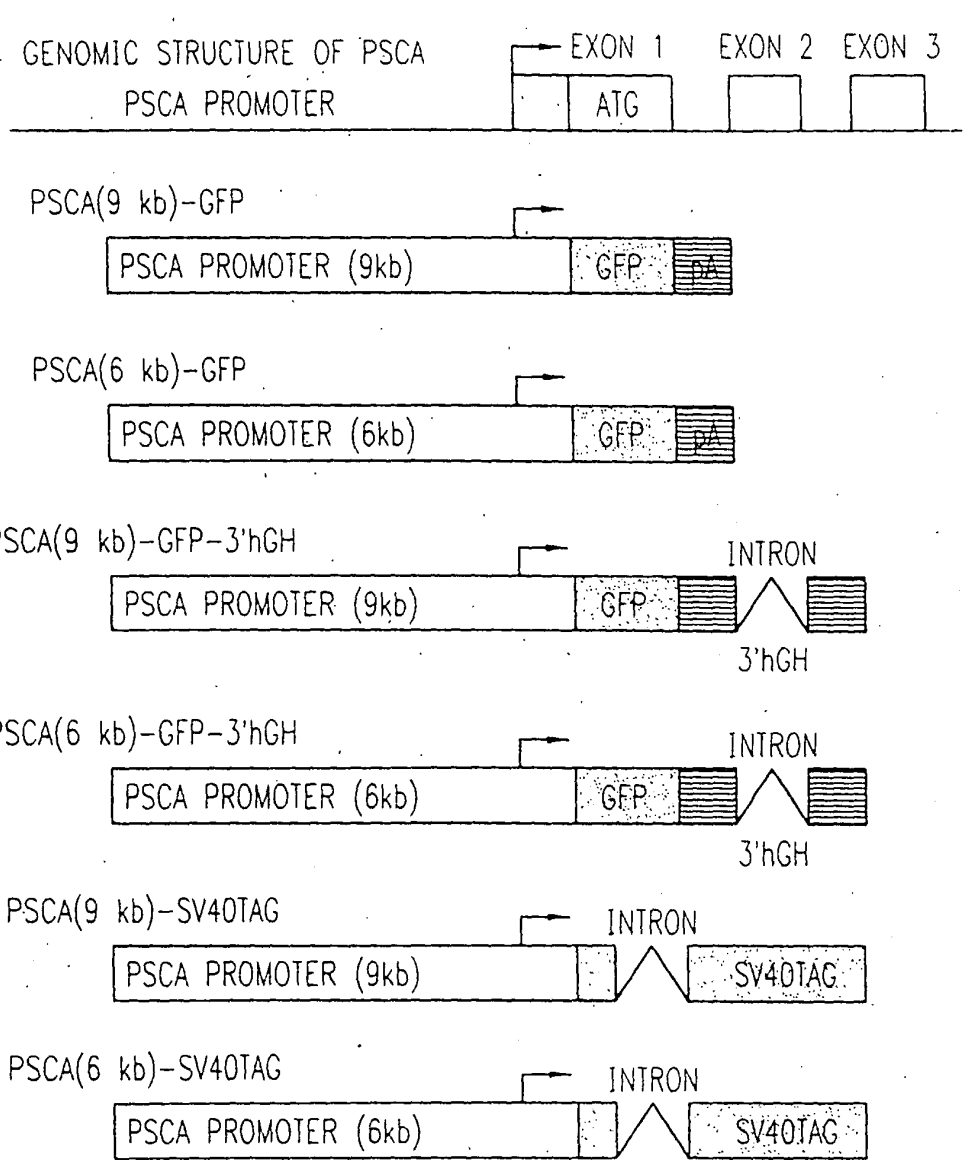

PrEC CELLS
(ANDROGEN-INDEPENDENT
PROSTATE BASAL CELLS)
PSCA PROMOTER
0 kb
1 kb
3 kb
6 kb
9 kb
LUC
0
5
10
RELATIVE LUCIFERASE ACTIVITY
TO CMV-LUC (%)
LNCoP CELLS
(ANDROGEN-DEPENDENT
PROSTATE SECRETORY CELLS)
0
5
10
RELATIVE LUCIFERASE ACTIVITY
TO CMV-LUC (%)

FIG. 44

FIG. 45



NUMBER OF FOUNDERS (DNA POSITIVE)
2
1
6
8
3
9

NEGATIVE TISSUES
STOMACH
SMALL INTESTINE
COLON
SEMINAL VESICLE
URETHRA
TESTIS
LIVER
KIDNEY
LUNG
BRAIN
HEART
SKELETAL MUSCLE
OVARY
UTERUS

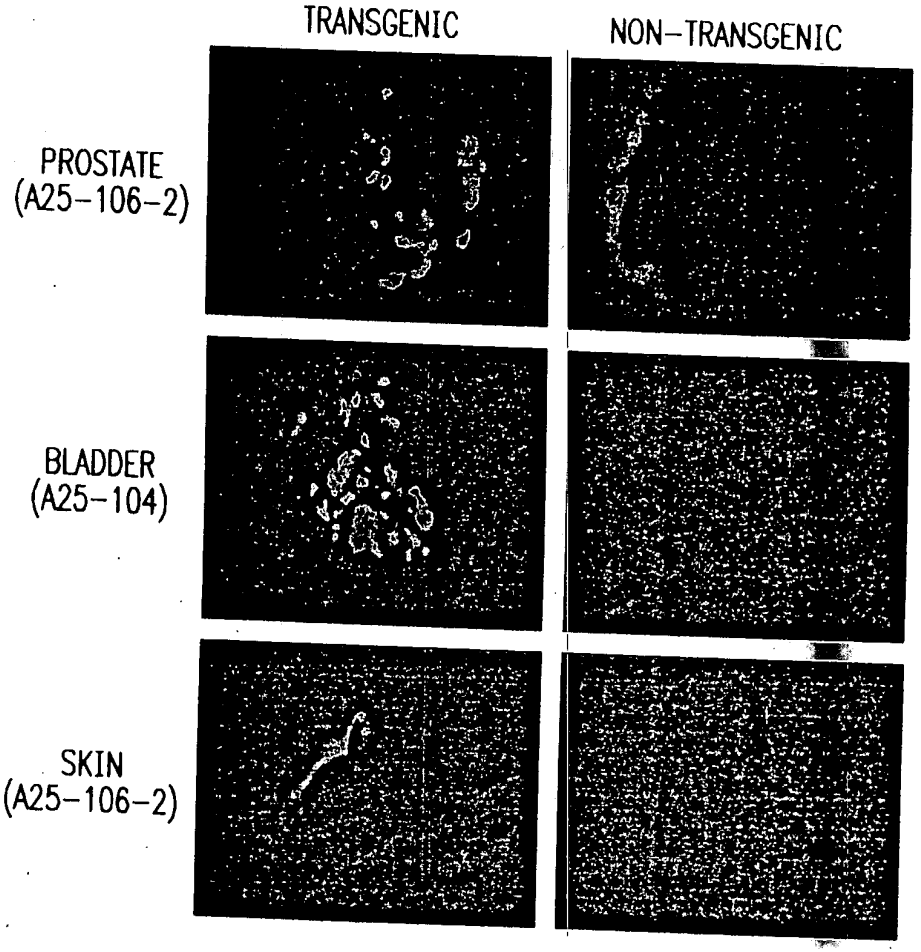


FIG. 46

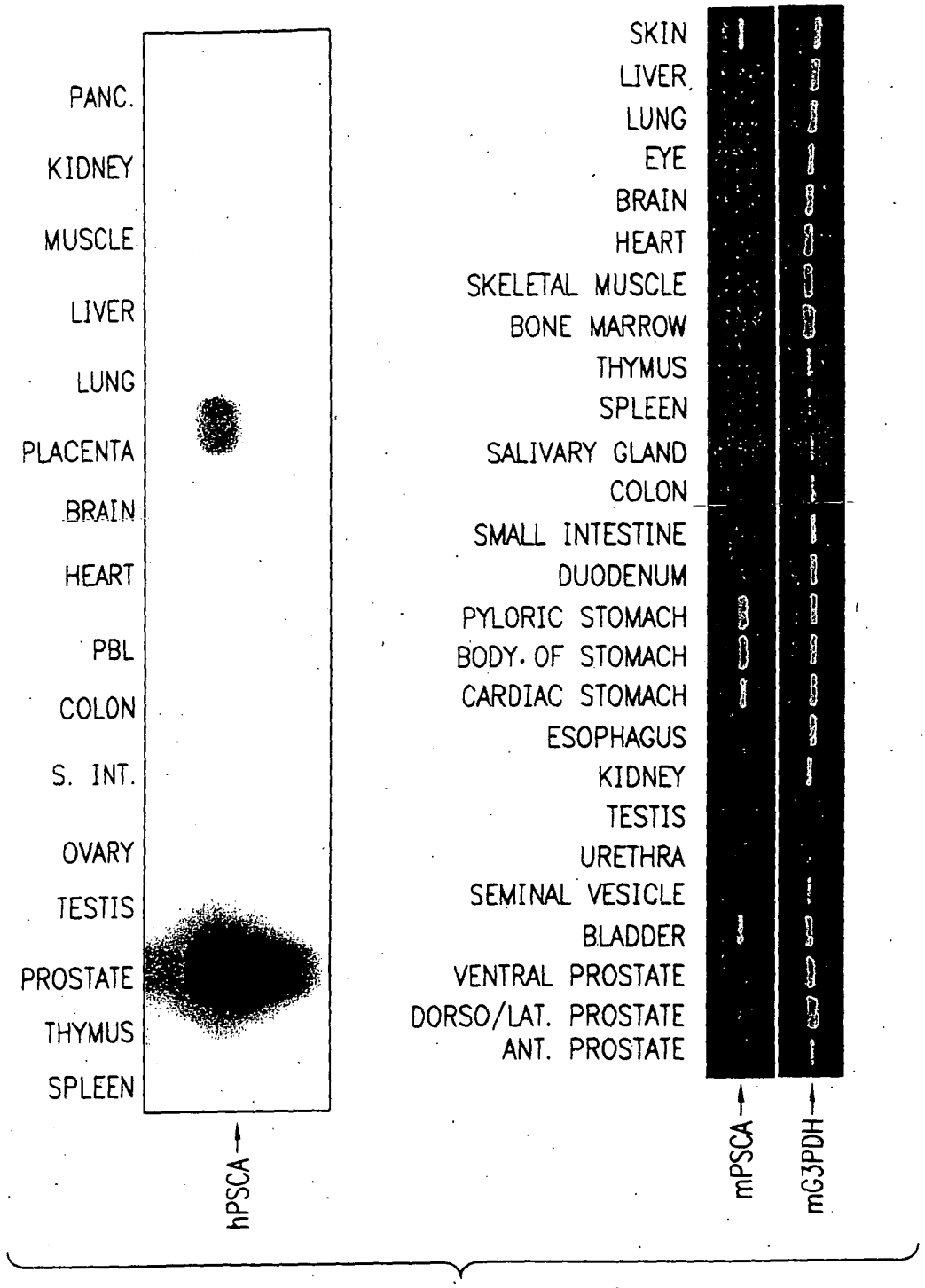
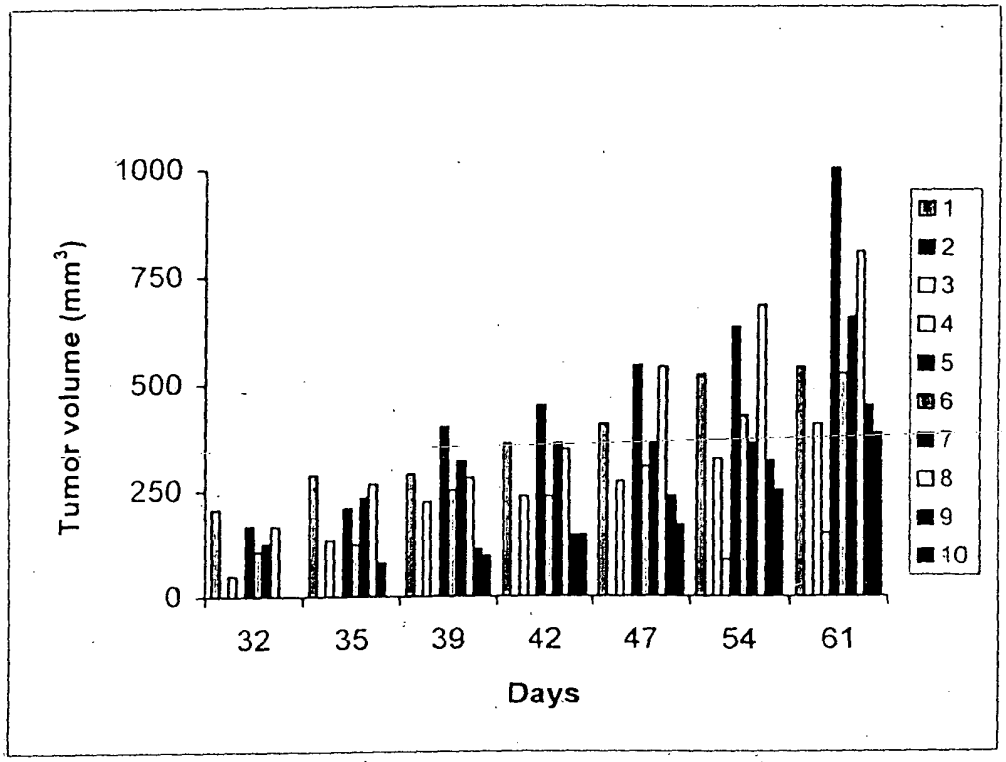


FIG. 47

FIG. 48



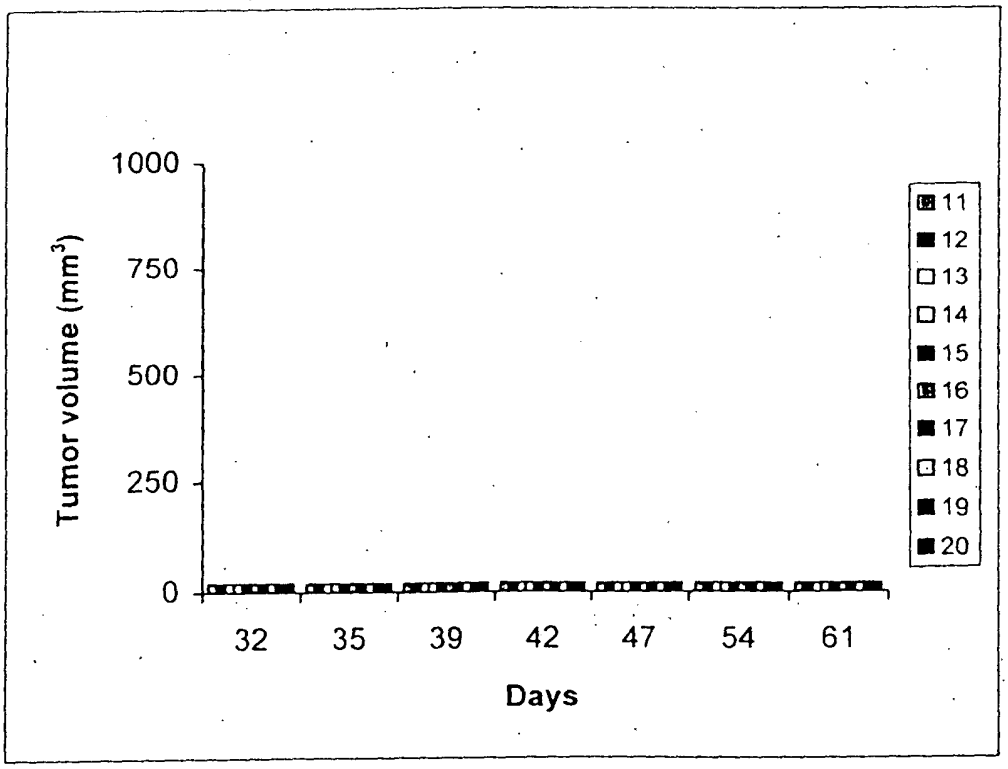


FIG. 49

A

mAb	Isotype	Epitope recognized (OD 450 nm) F (18-98)	N (2-50)	M (46-109)	C (85-123)
1G8	IgG1 k	**1.485**	0.004	**1.273**	0.003
2A2	IgG2a k	**0.973**	**0.631**	0.023	0.010
2H9	IgG1 k	**1.069**	**1.026**	0.002	0.001
3C5	IgG2a k	**1.916**	**1.709**	0.006	0.002
3E6	IgG3 k	**1.609**	0.036	**1.133**	**2.118**
3G3	IgG2a k	**2.805**	**1.731**	0.004	0.000
4A10	IgG2a k	**1.053**	**0.493**	0.000	0.001

B

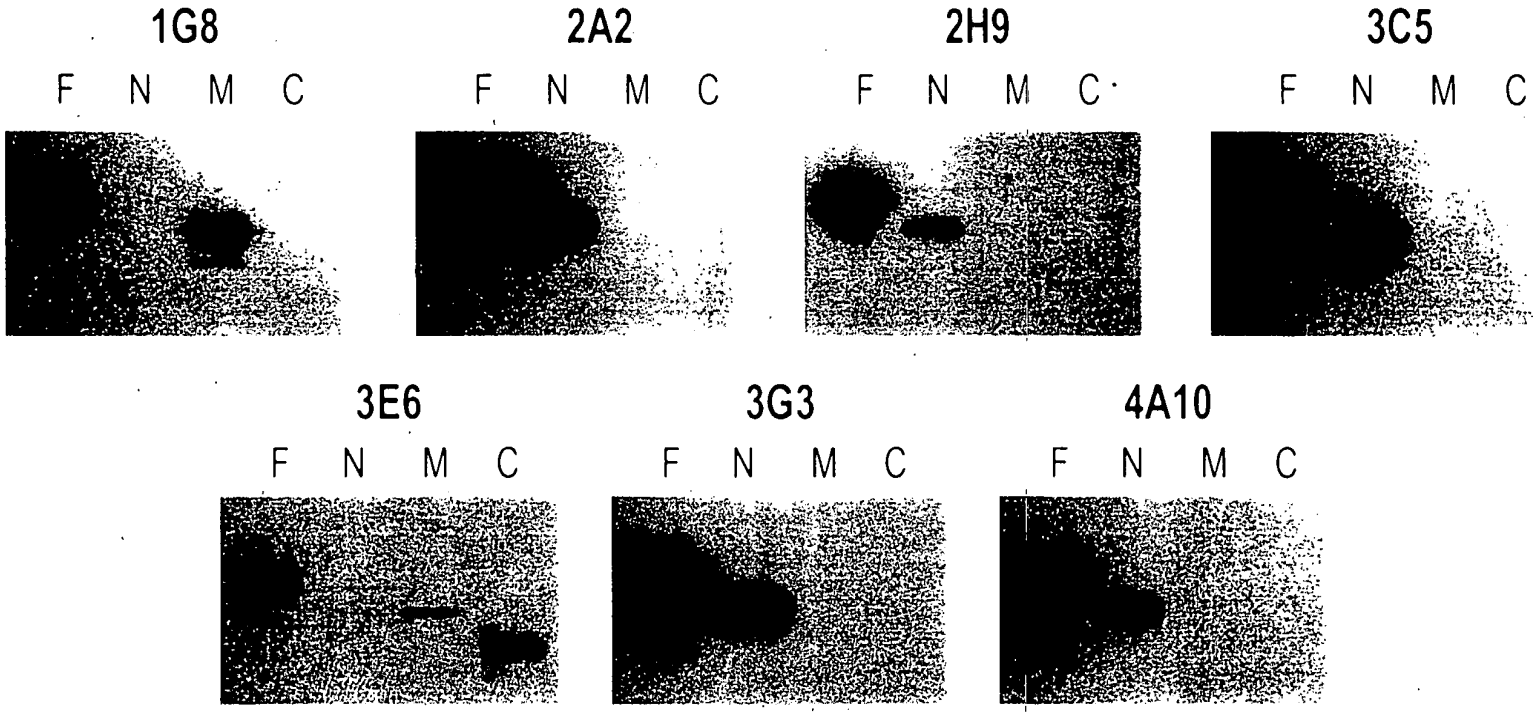


FIG. 50

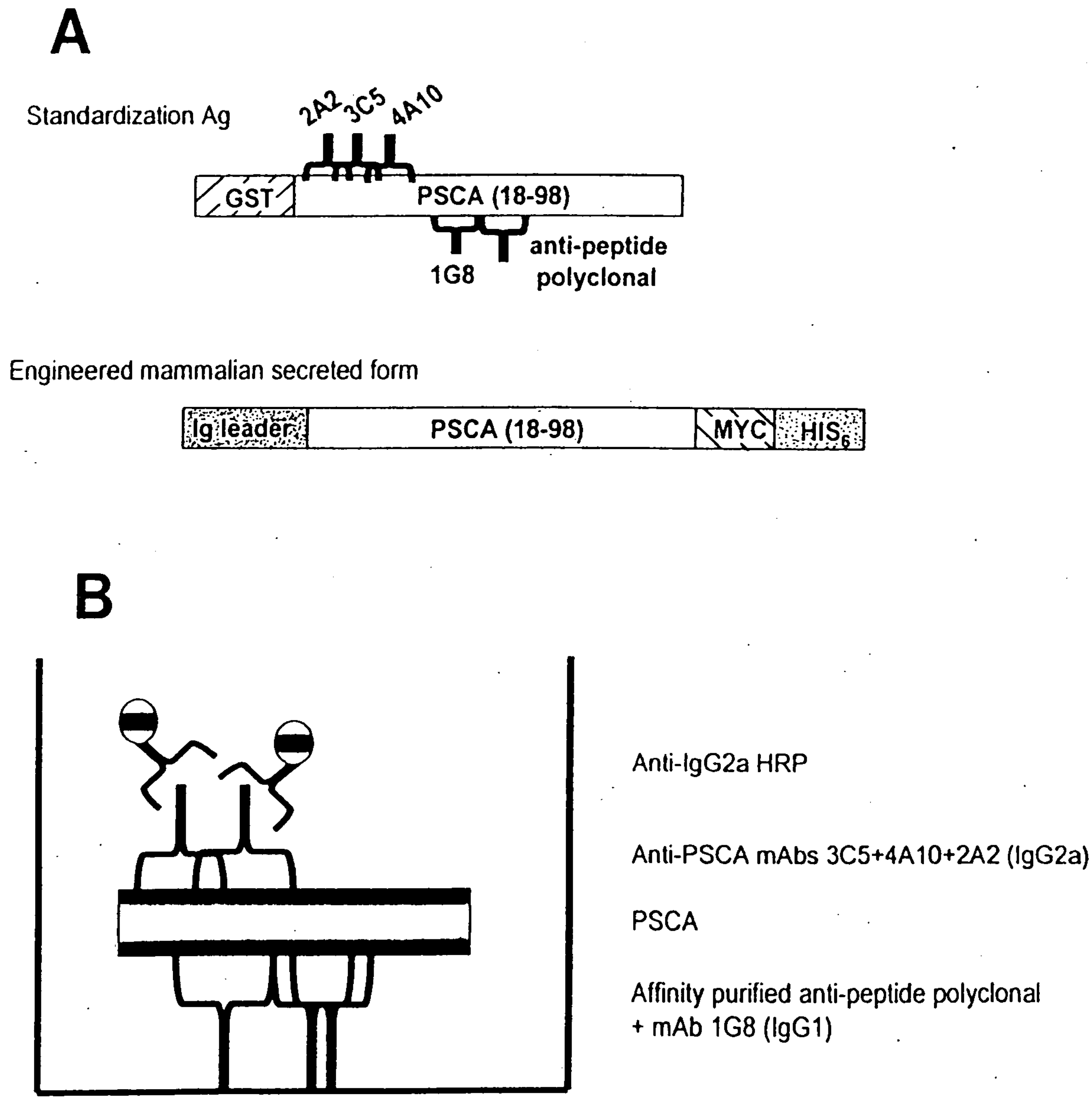
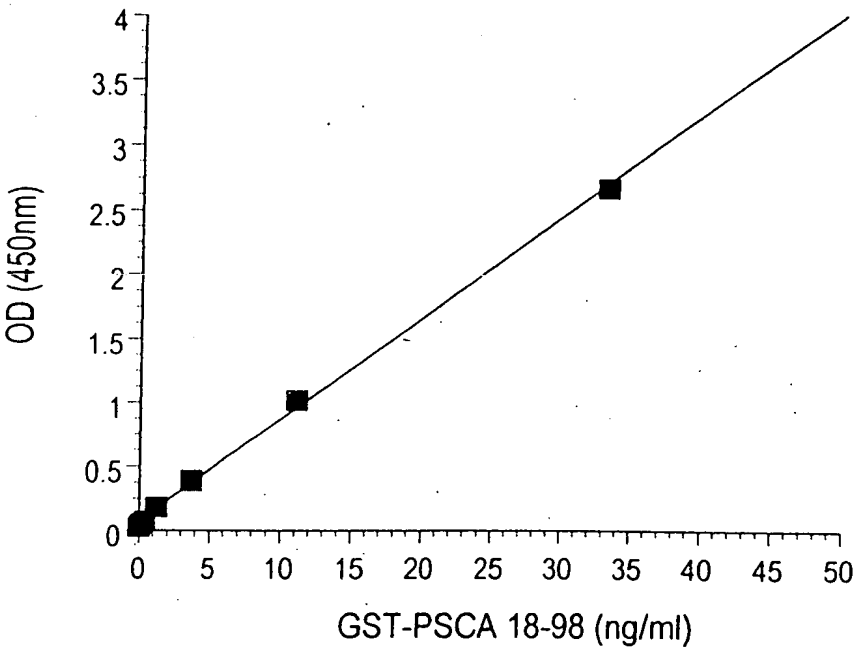

A
Standardization Ag
2A2
3C5
4A10
GST
PSCA (18-98)
1G8
anti-peptide
polyclonal
Engineered mammalian secreted form
Ig leader
PSCA (18-98)
MYC
HIS6
B
Anti-IgG2a HRP
Anti-PSCA mAbs 3C5+4A10+2A2 (IgG2a)
PSCA
Affinity purified anti-peptide polyclonal
+ mAb 1G8 (IgG1)

FIG. 51

A



B

Sample	OD+range (n=2)	ng/ml
vector	0.005+0.001	ND
vector+hu serum	0.004+0.001	ND
secPSCA	2.695+0.031	32.92
secPSCA+hu serum	2.187+0.029	26.55

FIG. 52

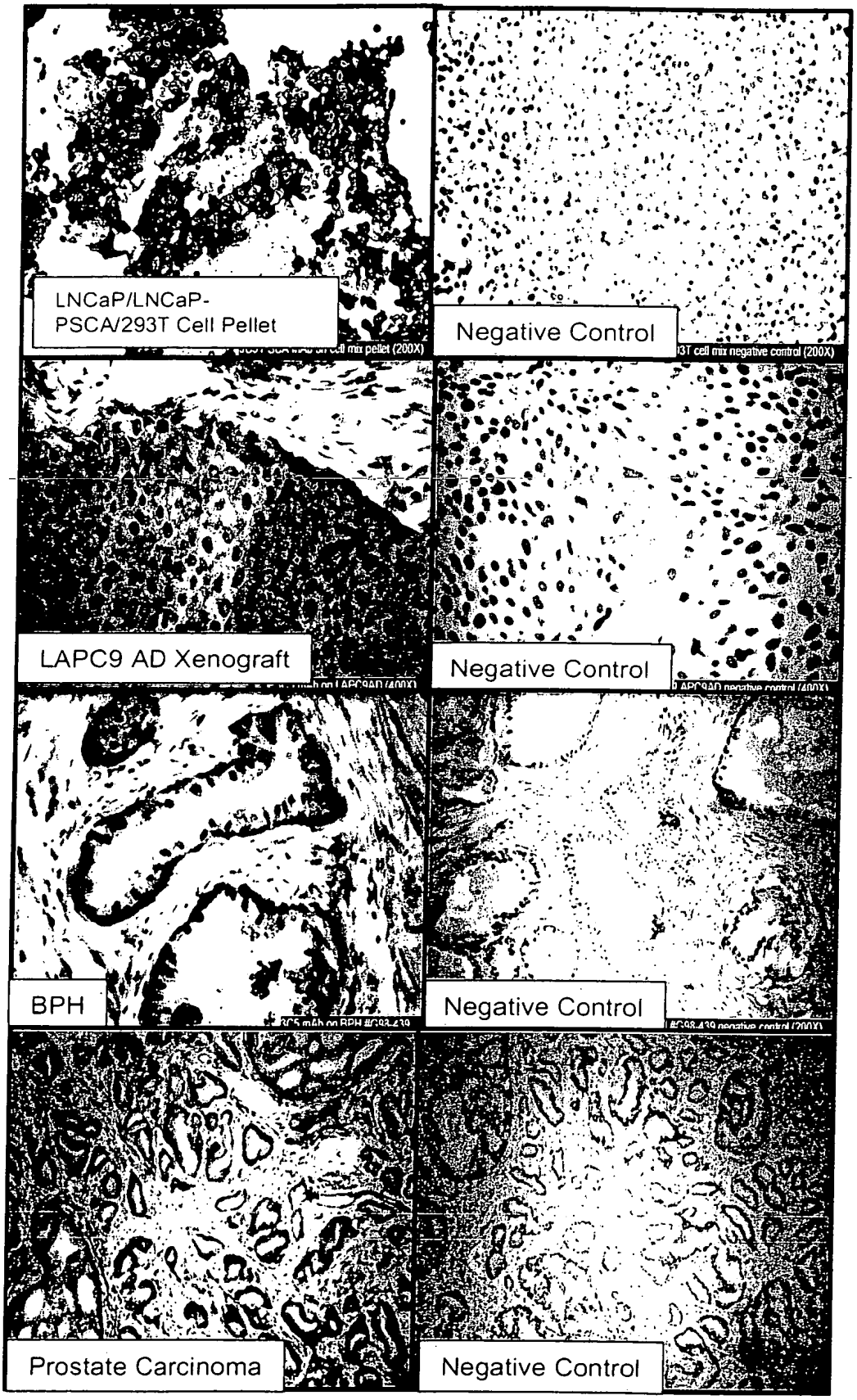
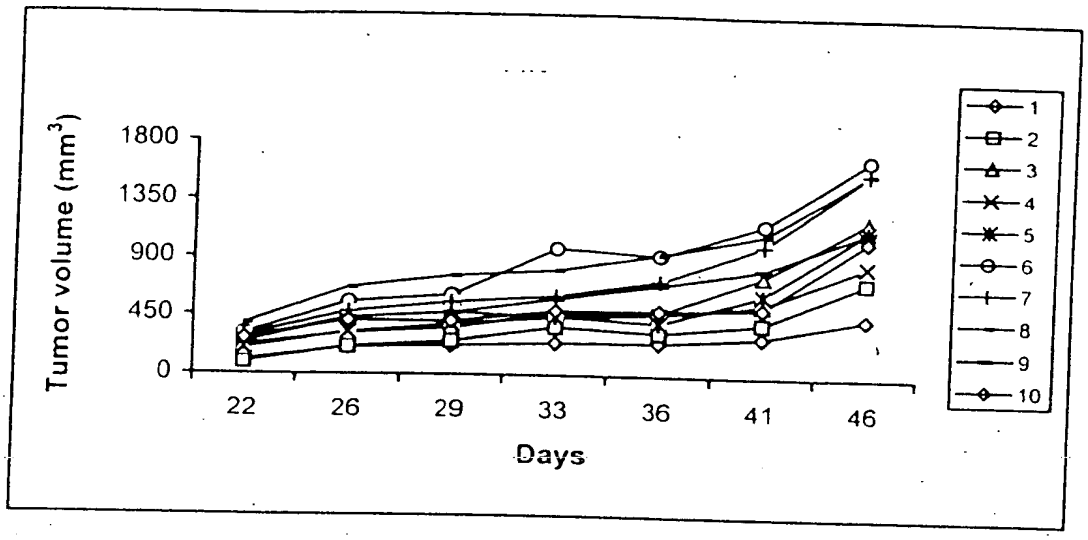
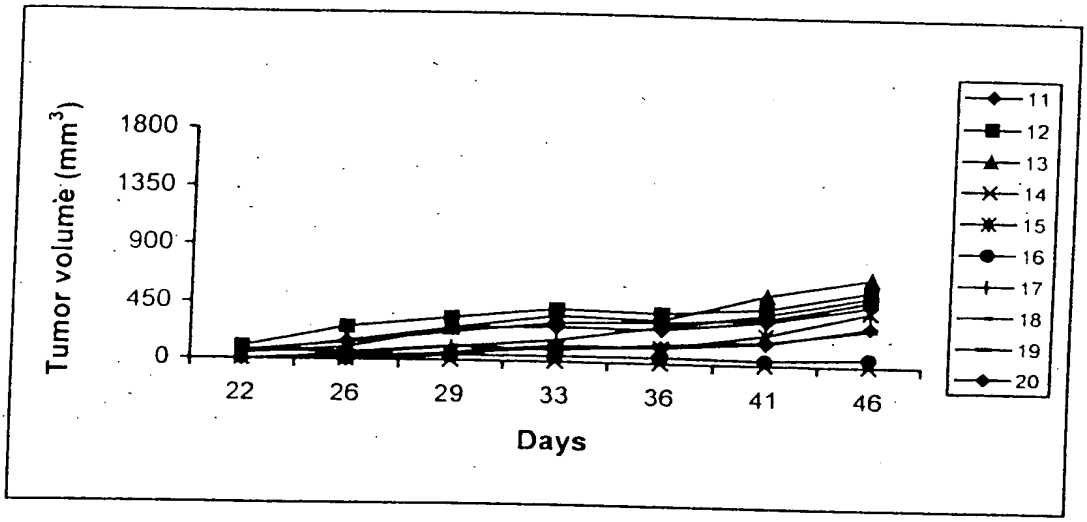

LNCaP/LNCaP-PSCA/293T Cell Pellet
Negative Control
LAPC9 AD Xenograft
Negative Control
BPH
Negative Control
Prostate Carcinoma
Negative Control

FIG. 53


Tumor volume (mm3)
1800
1350
900
450
0
22
26
29
33
36
41
46
Days
1
2
3
4
5
6
7
8
9
10


Tumor volume (mm3)
1800
1350
900
450
0
22
26
29
33
36
41
46
Days
11
12
13
14
15
16
17
18
19
20

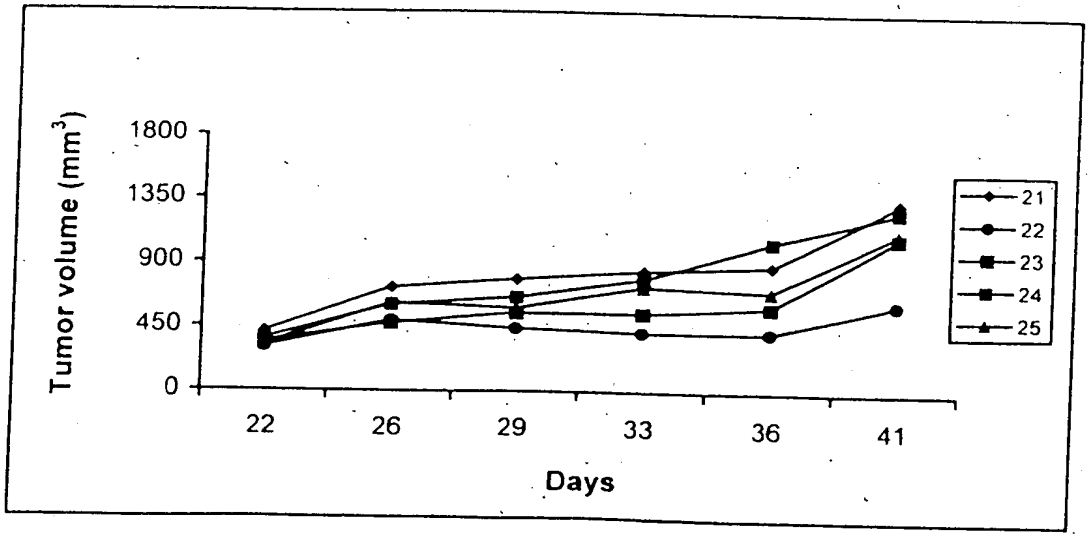
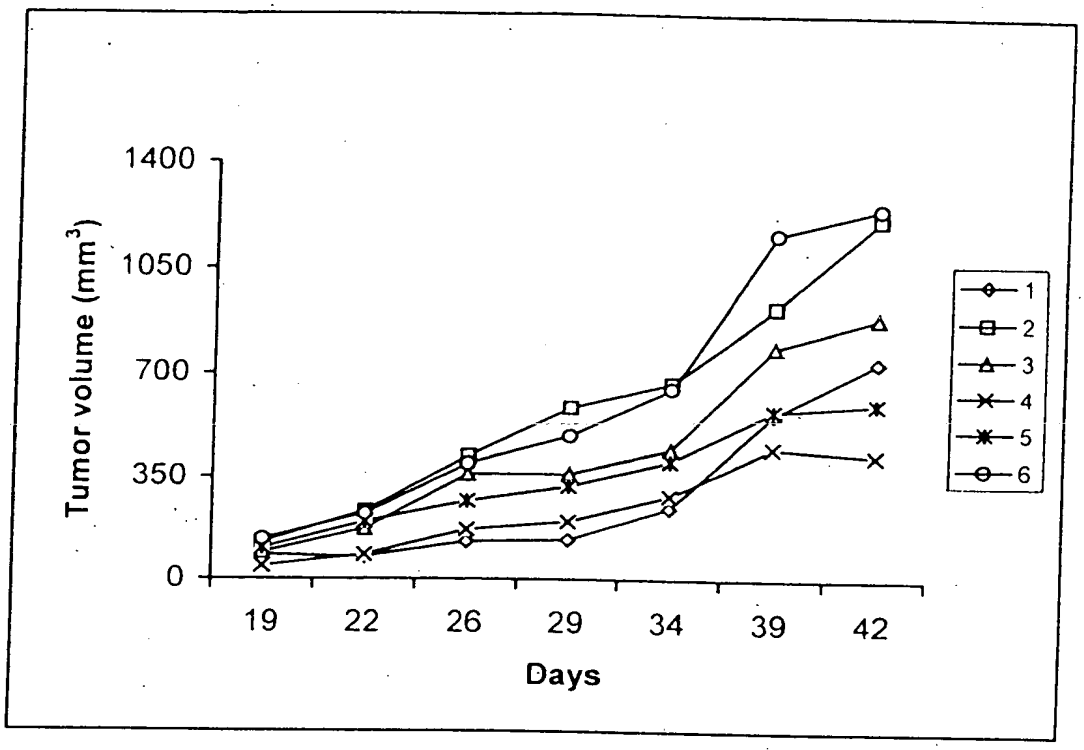

Tumor volume (mm3)
1800
1350
900
450
0
22
26
29
33
36
41
Days
21
22
23
24
25

FIG. 54


1400
1050
700
350
0
Tumor volume (mm3)
19
22
26
29
34
39
42
Days
1
2
3
4
5
6

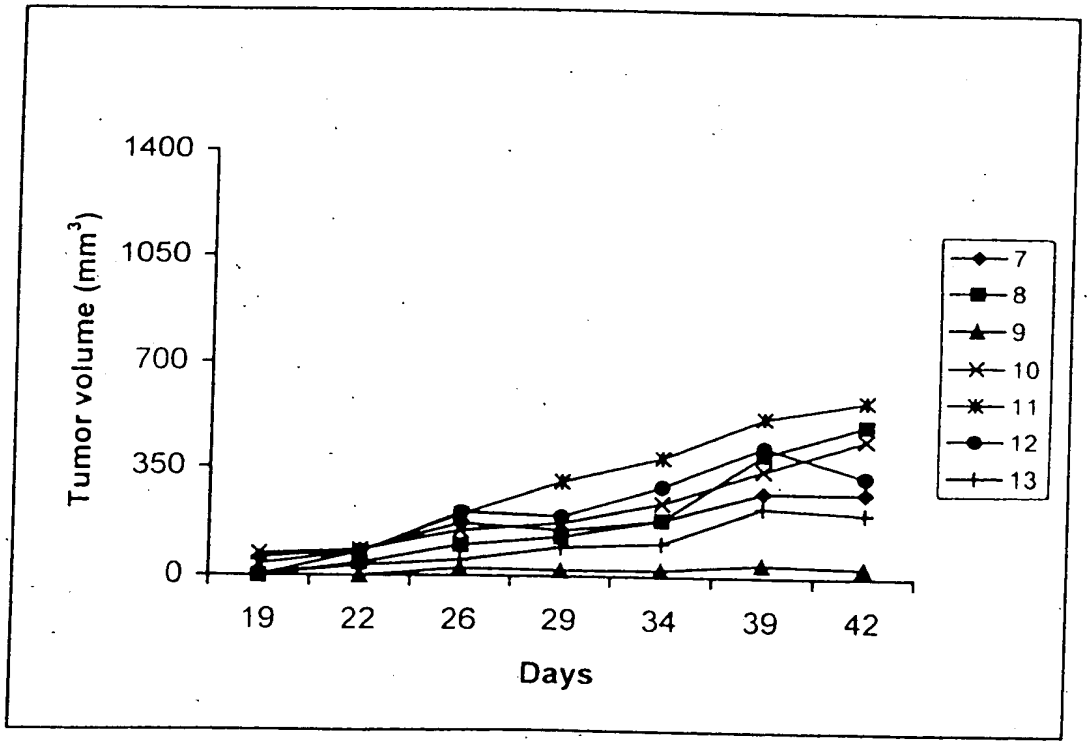
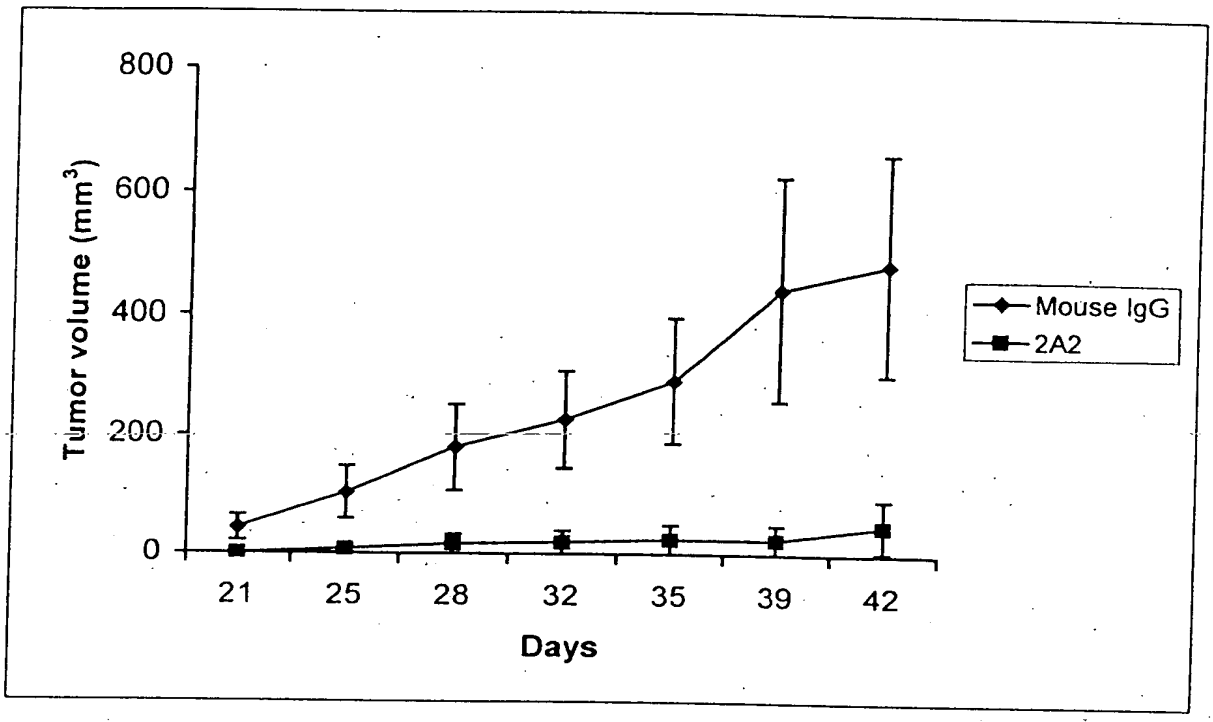

1400
1050
700
350
0
Tumor volume (mm3)
19
22
26
29
34
39
42
Days
7
8
9
10
11
12
13

FIG. 55


800
600
400
200
0
Tumor volume (mm3)
21
25
28
32
35
39
42
Days
Mouse IgG
2A2

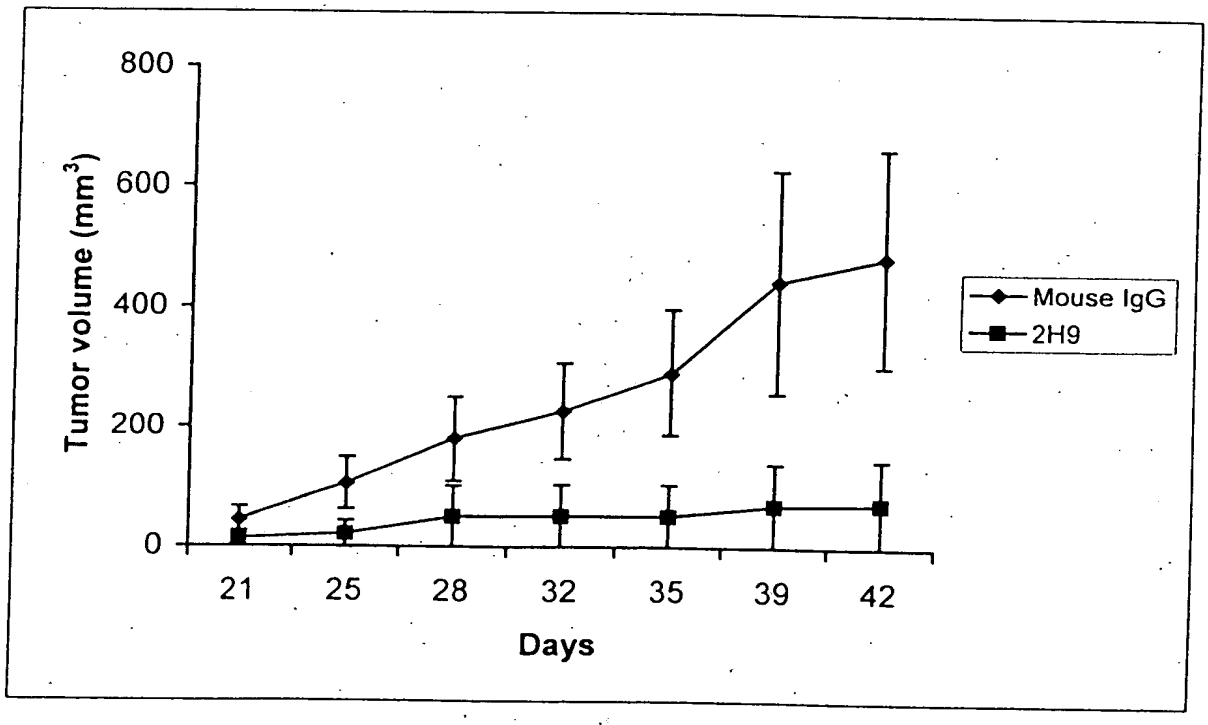
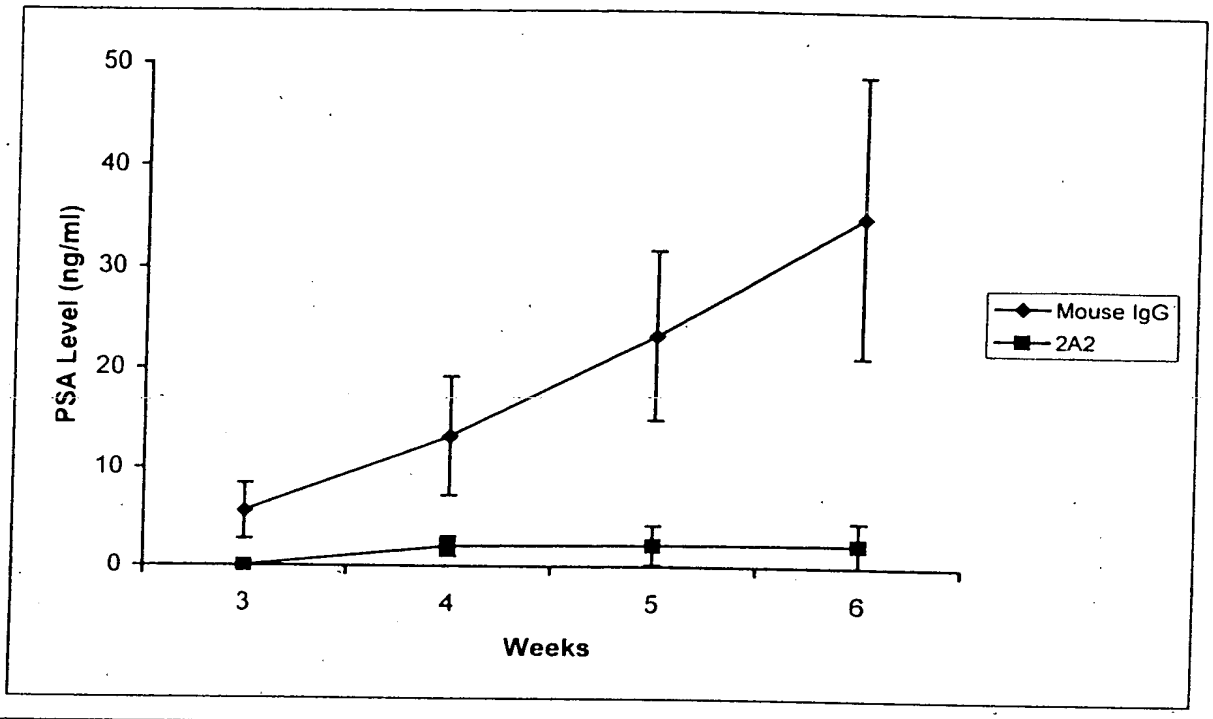

800
600
400
200
0
Tumor volume (mm3)
21
25
28
32
35
39
42
Days
Mouse IgG
2H9

FIG. 56


50
40
30
20
10
0
PSA Level (ng/ml)
3
4
5
6
Weeks
Mouse IgG
2A2

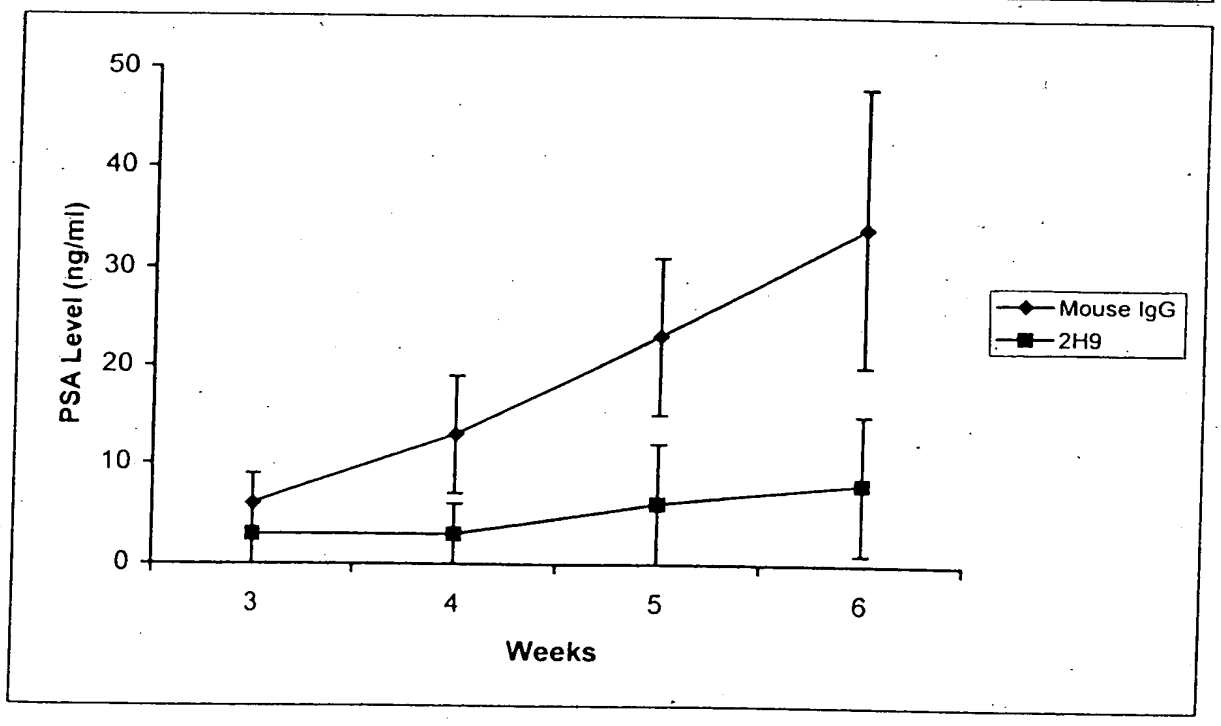

50
40
30
20
10
0
PSA Level (ng/ml)
3
4
5
6
Weeks
Mouse IgG
2H9

FIG. 57

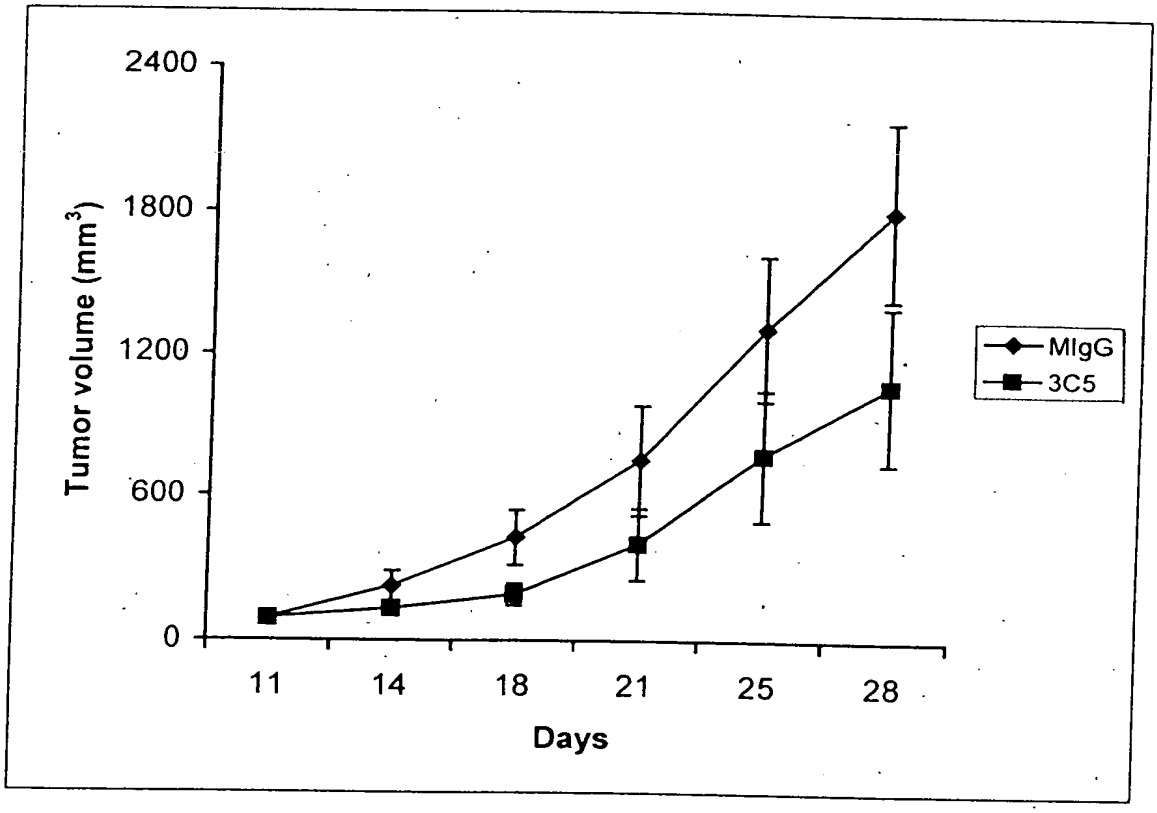

2400
1800
1200
600
0
Tumor volume (mm3)
11
14
18
21
25
28
Days
MIgG
3C5

FIG. 58

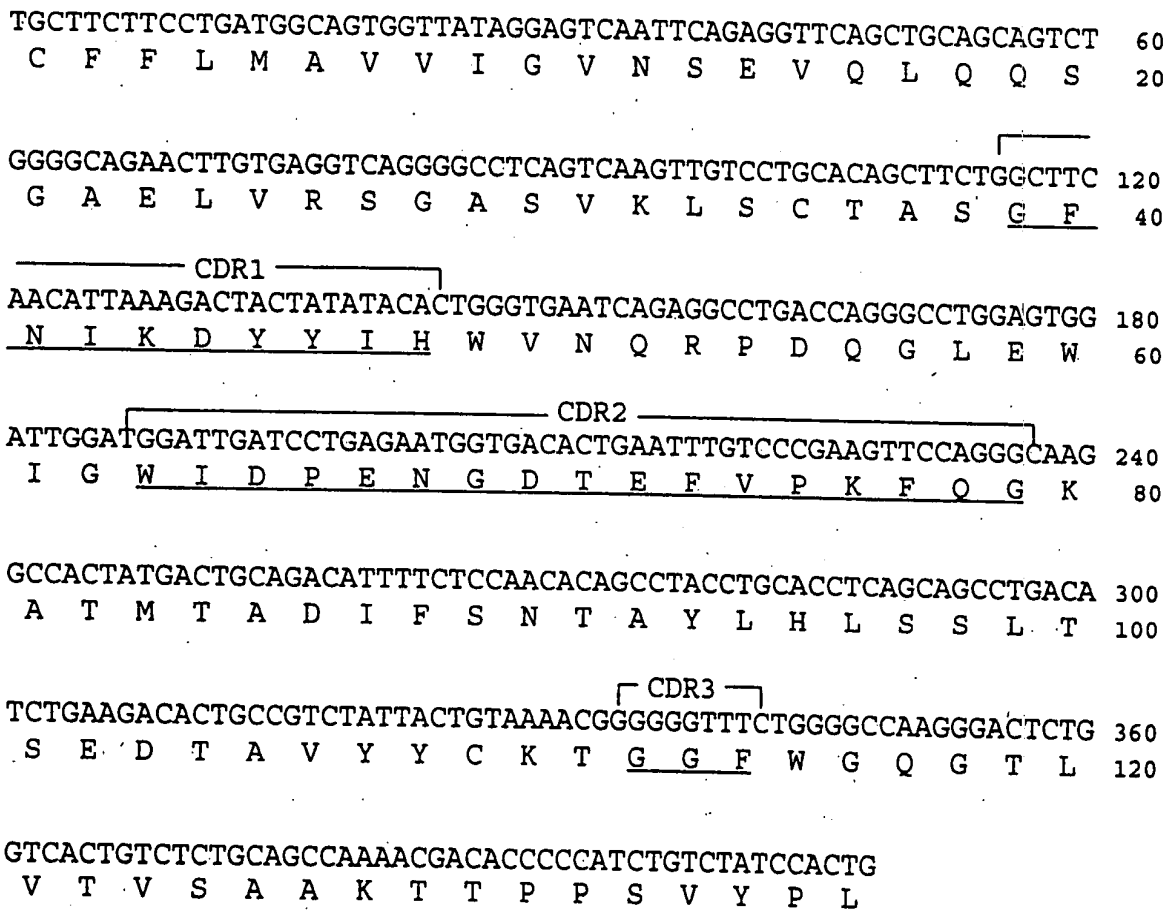


FIG. 59

```
TTGGTAGCAACAGCCTCAGATGTCCACTCCCAGGTCCAACTGCAGCAACCTGGGTCTGAA  60
 L  V  A  T  A  S  D  V  H  S  Q  V  Q  L  Q  Q  P  G  S  E   20

CTGGTGAGGCCTGGAACTTCAGTGAAGCTGTCCTGCAAGGCTTCTGGCTATACATTCTCC 120
 L  V  R  P  G  T  S  V  K  L  S  C  K  A  S  G  Y  T  F  S   40
                                                    CDR1

AGCTACTGGATGCACTGGGTGAAGCAGAGGCCTGGACAAGGCCTTGAGTGGATTGGAAAT 180
 S  Y  W  M  H  W  V  K  Q  R  P  G  Q  G  L  E  W  I  G  N   60

ATTGACCCTGGTAGTGGTTACACTAACTACGCTGAGAACCTCAAGACCAAGGCCACACTG 240
 I  D  P  G  S  G  Y  T  N  Y  A  E  N  L  K  T  K  A  T  L   80
                CDR2

ACTGTAGACACATCCTCCAGCACAGCCTACATGCAGCTCAGCAGCCTGACATCTGAGGAC 300
 T  V  D  T  S  S  S  T  A  Y  M  Q  L  S  S  L  T  S  E  D  100

TCTGCAGTCTATTACTGTACAAGCCGATCTACTATGATTACGACGGGATTTGCTTACTGG 360
 S  A  V  Y  Y  C  T  S  R  S  T  M  I  T  T  G  F  A  Y  W  120
                            CDR3

GGCCAAGGGACTCTGGTCACTGTCTCTGCAGCTACAACAACAGCCCCATCTGTCTATCCA 420
 G  Q  G  T  L  V  T  V  S  A  A  T  T  T  A  P  S  V  Y  P  160

CTGGCC
 L  A
```

FIG. 60

```
AATGACTTCGGGTTGAGCTGGGTTTTTATTATTGTTCTTTTAAAAGGGGTCCGGAGTGAA  60
 N  D  F  G  L  S  W  V  F  I  I  V  L  L  K  G  V  R  S  E   20

GTGAGGCTTGAGGAGTCTGGAGGAGGCTGGGTGCAACCTGGAGGATCCATGAAACTCTCC 120
 V  R  L  E  E  S  G  G  G  W  V  Q  P  G  G  S  M  K  L  S   40

TGTGTAGCCTCTGGATTTACTTTCAGTAATTACTGGATGACTTGGGTCCGCCAGTCTCCA 180
 C  V  A  S  G  F  T  F  S  N  Y  W  M  T  W  V  R  Q  S  P   60
                        CDR1

GAGAAGGGGCTTGAGTGGGTTGCTGAAATTCGATTGAGATCTGAAAATTATGCAACACAT 240
 E  K  G  L  E  W  V  A  E  I  R  L  R  S  E  N  Y  A  T  H   80
                                                 CDR2

TATGCGGAGTCTGTGAAAGGGAAATTCACCATCTCAAGAGATGATTCCAGAAGTCGTCTC 300
 Y  A  E  S  V  K  G  K  F  T  I  S  R  D  D  S  R  S  R  L  100

TACCTGCAAATGAACAACTTAAGACCTGAAGACAGTGGAATTTATTACTGTACAGATGGT 360
 Y  L  Q  M  N  N  L  R  P  E  D  S  G  I  Y  Y  C  T  D  G  120

CTGGGACGACCTAACTGGGGCCAAGGGACTCTGGTCACTGTCTCTGCAGCCAAAACGACA 420
 L  G  R  P  N  W  G  Q  G  T  L  V  T  V  S  A  A  K  T  T  140
    CDR3

CCCCCATCTGTCTATCCACTGGCCCCTTGTGTA
 P  P  S  V  Y  P  L  A  P  C  V
```

FIG. 61

CDR1 Comparisons

1G8	$1gG_{1k}$	Middle	G	F	N	I	K	D	Y	Y	I	H
2H9	$1gG_{1k}$	N-Term.	G	F	T	F	S	N	Y	W	M	T
4A10	$1gG_{2ak}$	N-Term.	G	Y	T	F	S	S	Y	W	M	H

CDR2 Comparisons

1G8	$1gG_{1k}$	W	I	D	P	E	N	G	D	T	E	F	V	P	K	F	Q	G
2H9	$1gG_{1k}$	E	I	R	L	R	S	E	N	Y	A	T	H	Y	A	E	S	V	K	G
4A10	$1gG_{2ak}$	N	I	D	P	G	S	G	Y	T	N			Y	A	E	N	L	K	T

CDR3 Comparisons

1G8	$1gG_{1k}$	G	G	F								
2H9	$1gG_{1k}$	L	G	R	P	N						
4A10	$1gG_{2ak}$	R	S	T	M	I	T	T	G	F	A	Y

FIG. 62

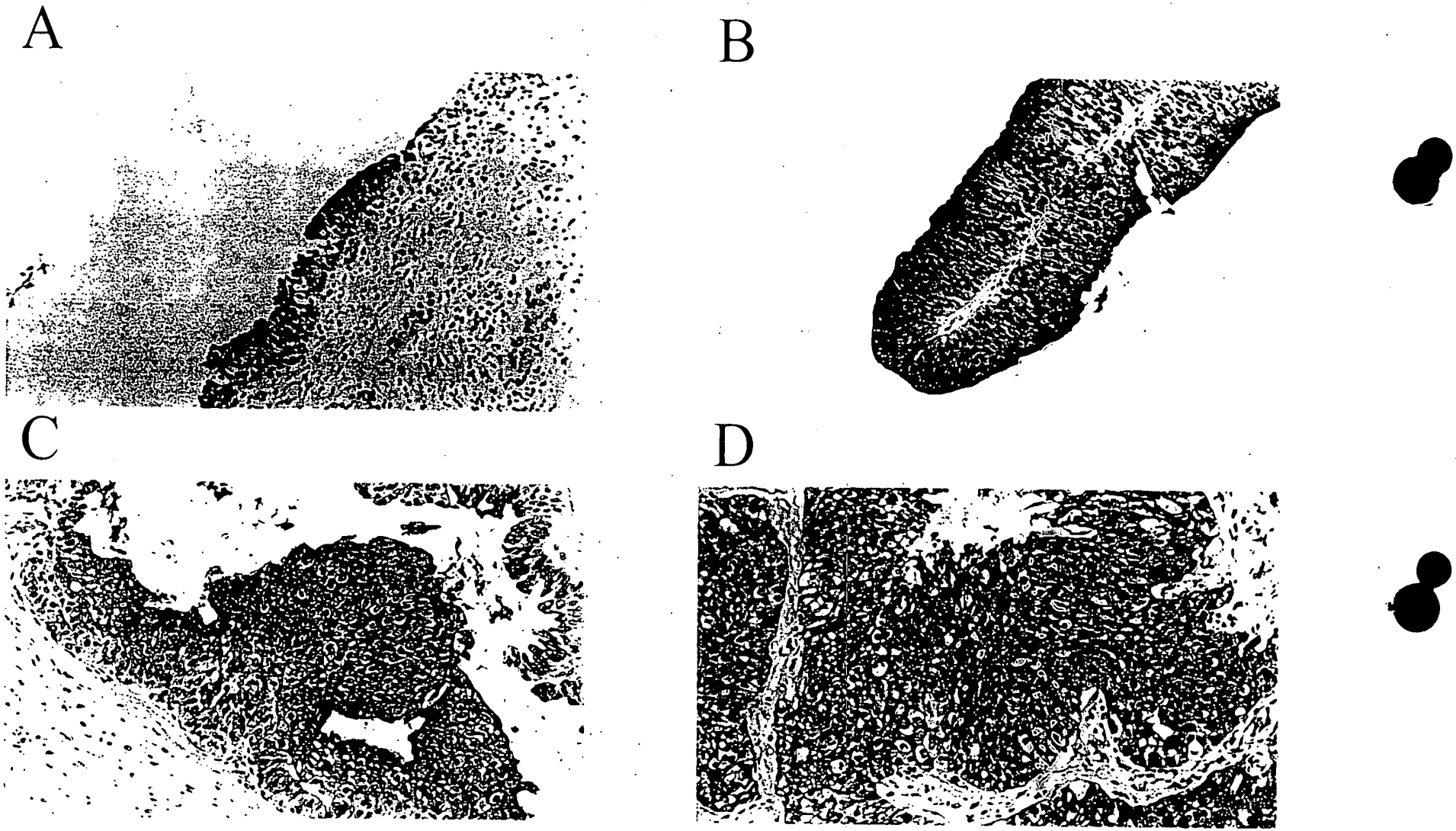


FIG. 63

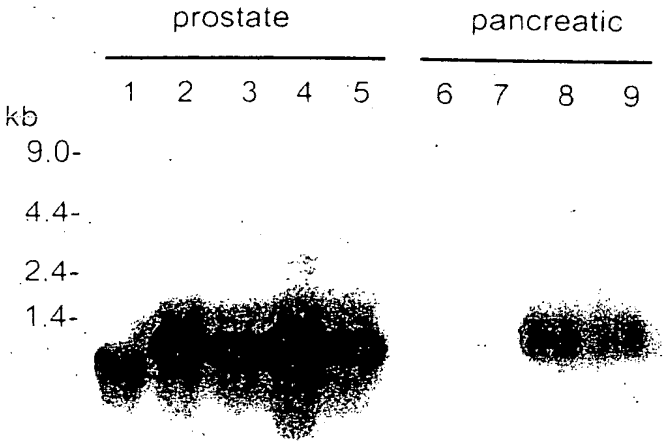


FIG. 64

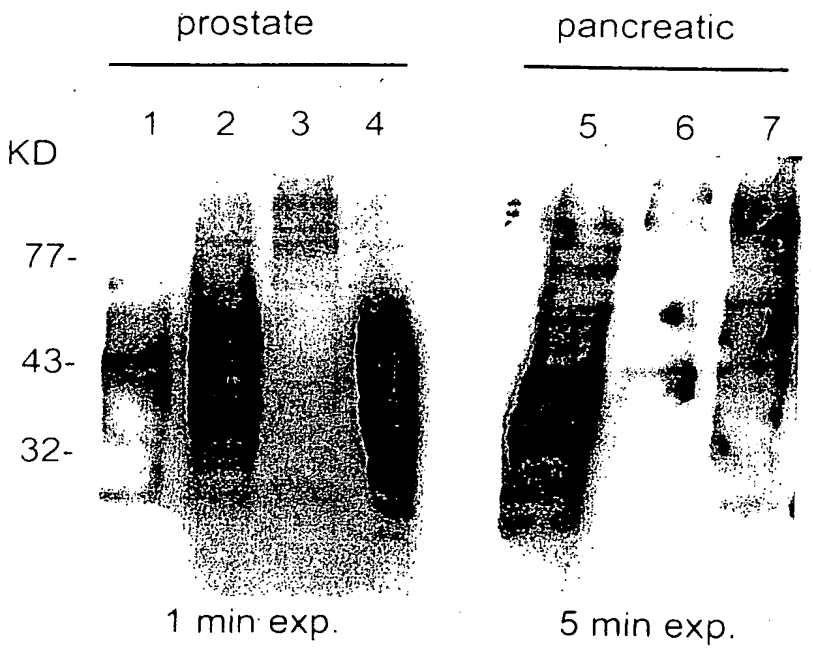
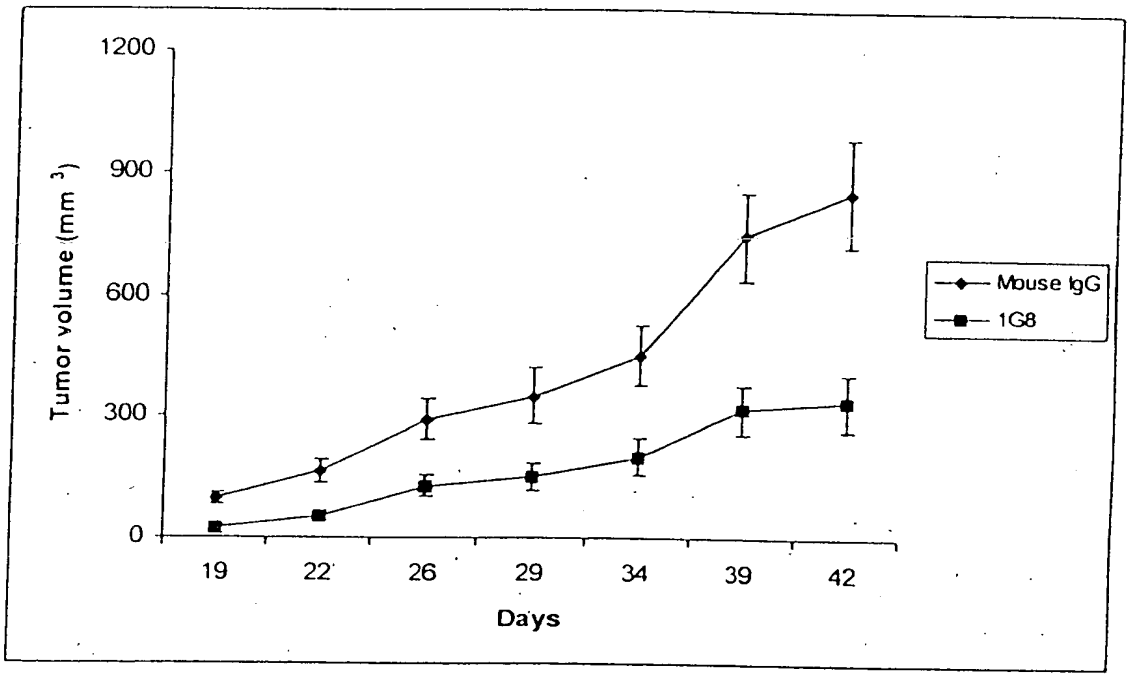


FIG. 65


1200
900
600
300
0
Tumor volume (mm 3)
19
22
26
29
34
39
42
Days
Mouse IgG
1G8

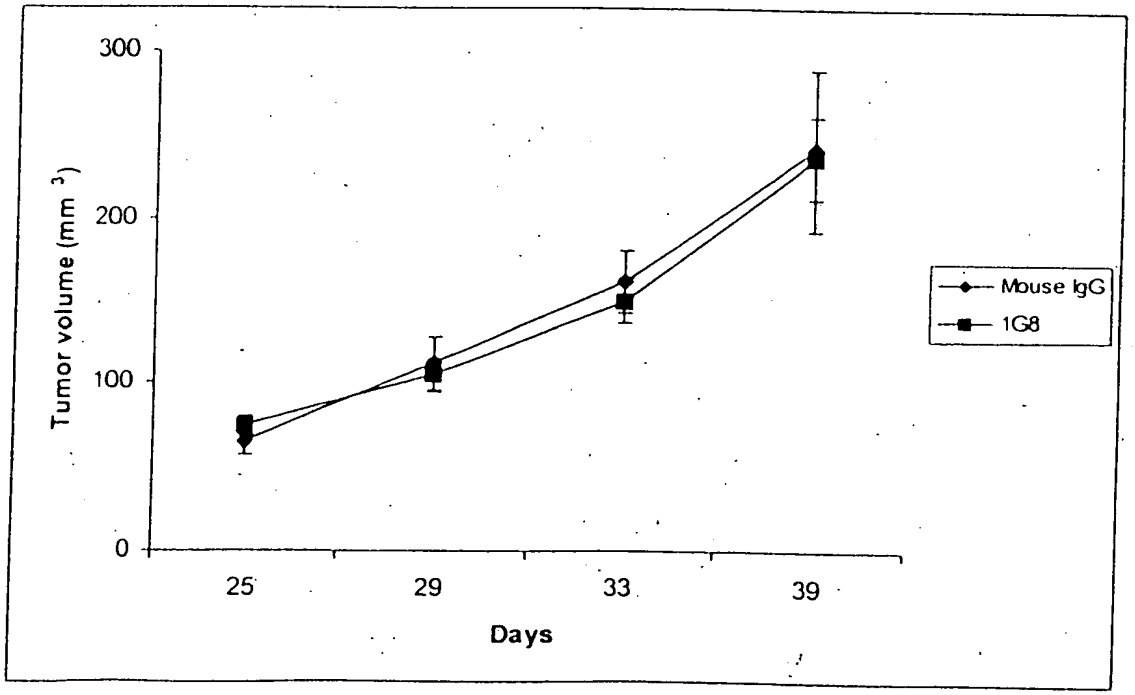
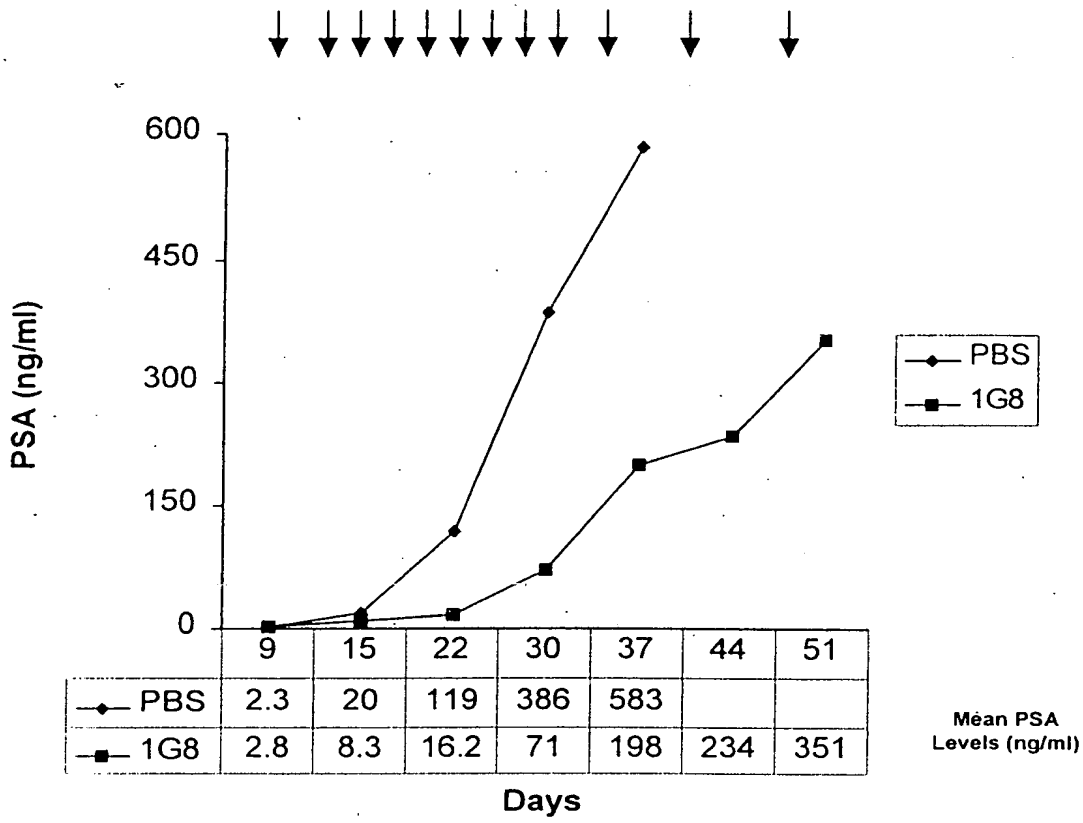

300
200
100
0
Tumor volume (mm 3)
25
29
33
39
Days
Mouse IgG
1G8

FIG. 66

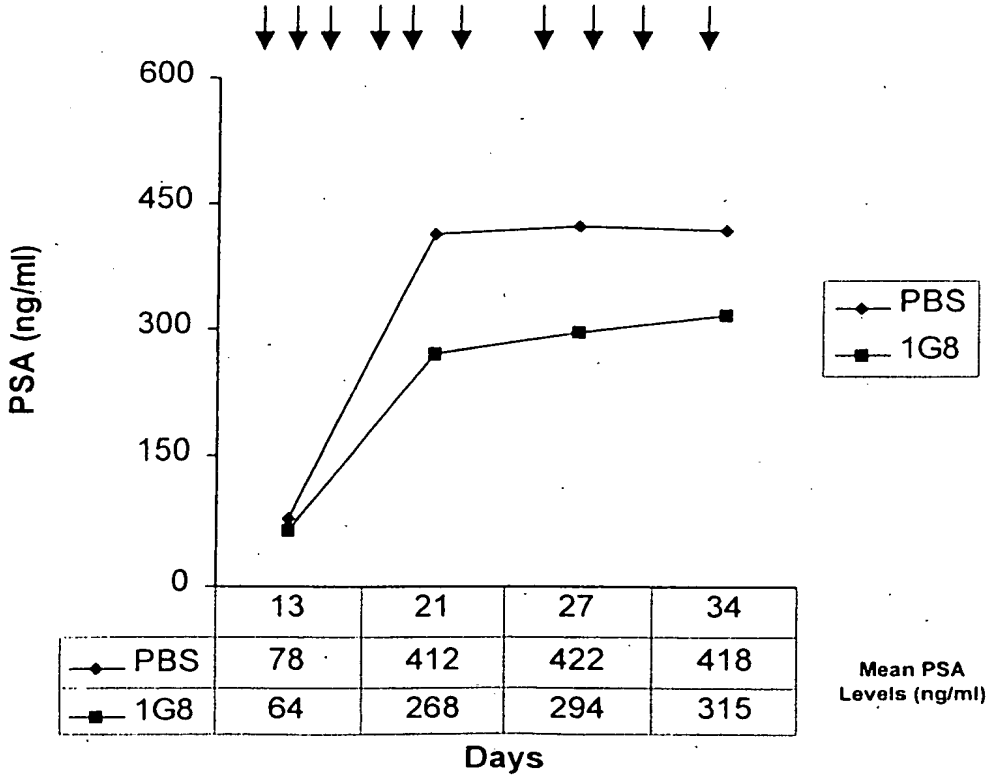
A)



	9	15	22	30	37	44	51
PBS	2.3	20	119	386	583		
1G8	2.8	8.3	16.2	71	198	234	351

Mean PSA Levels (ng/ml)

B)

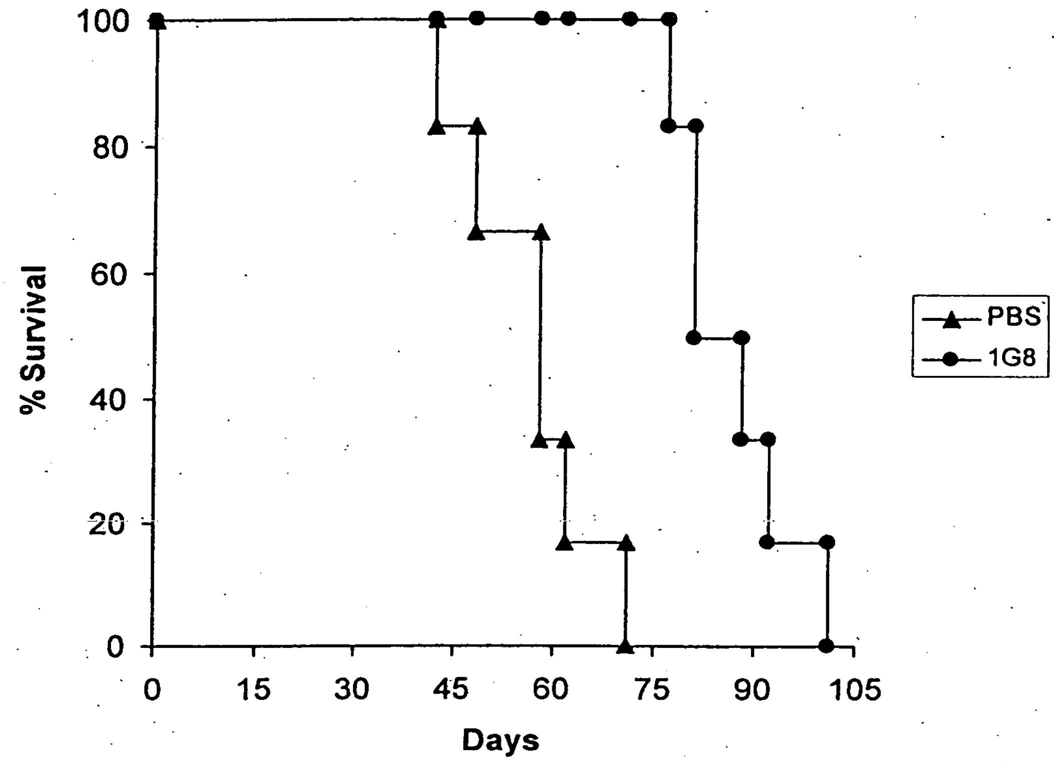


	13	21	27	34
PBS	78	412	422	418
1G8	64	268	294	315

Mean PSA Levels (ng/ml)

FIG. 67

A)



B)

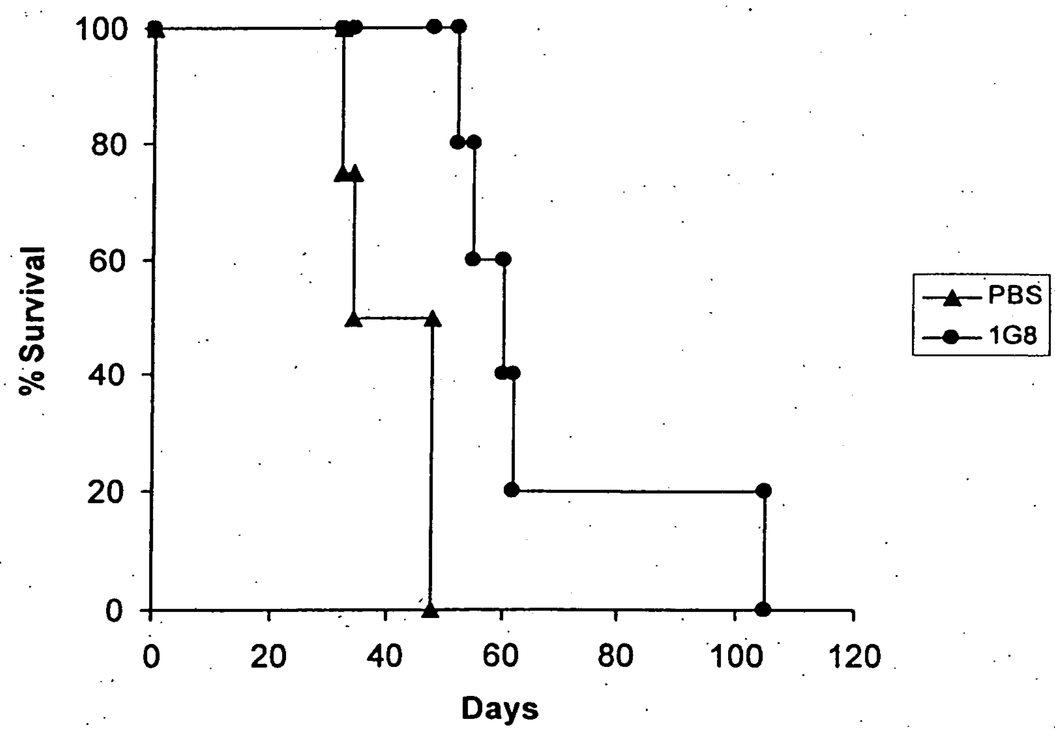
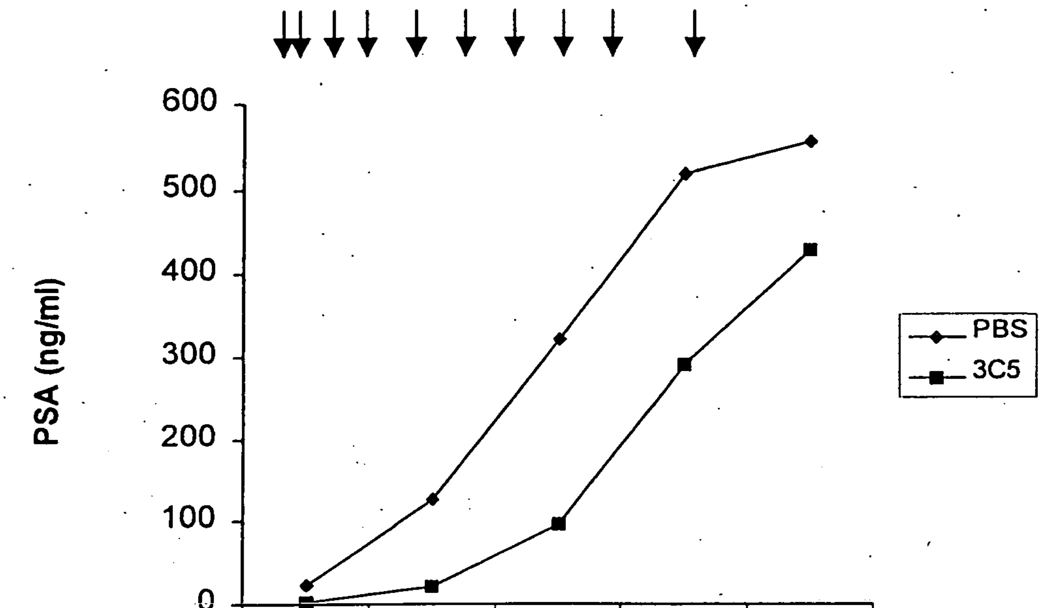


FIG. 68

A)

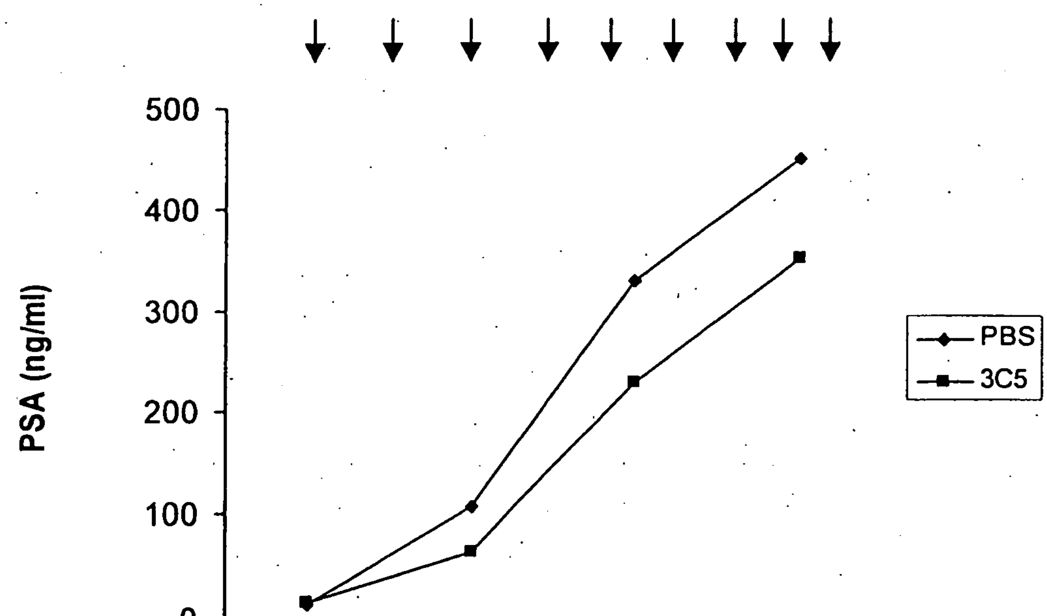


	9	16	22	29	36
PBS	23	126	322	519	555
3C5	3	21	95	290	428

Mean PSA Levels (ng/ml)

Days

B)



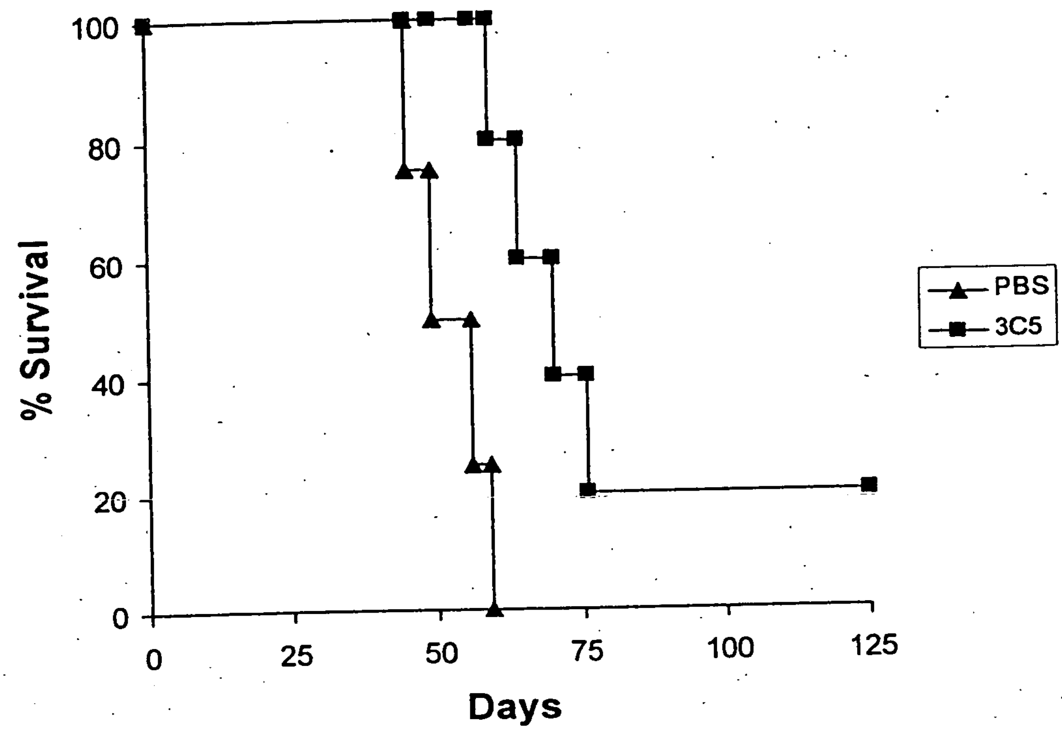
	7	14	21	28
PBS	14	107	329	449
3C5	16	63	229	351

Mean PSA Levels (ng/ml)

Days

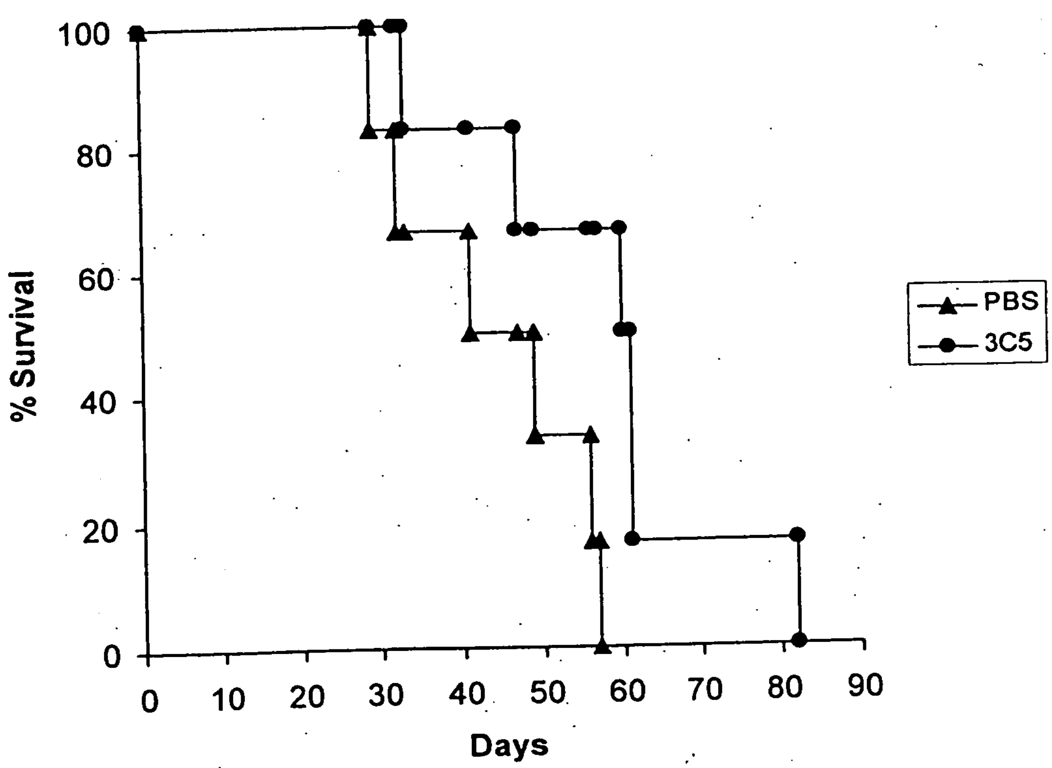
FIG. 69

A)



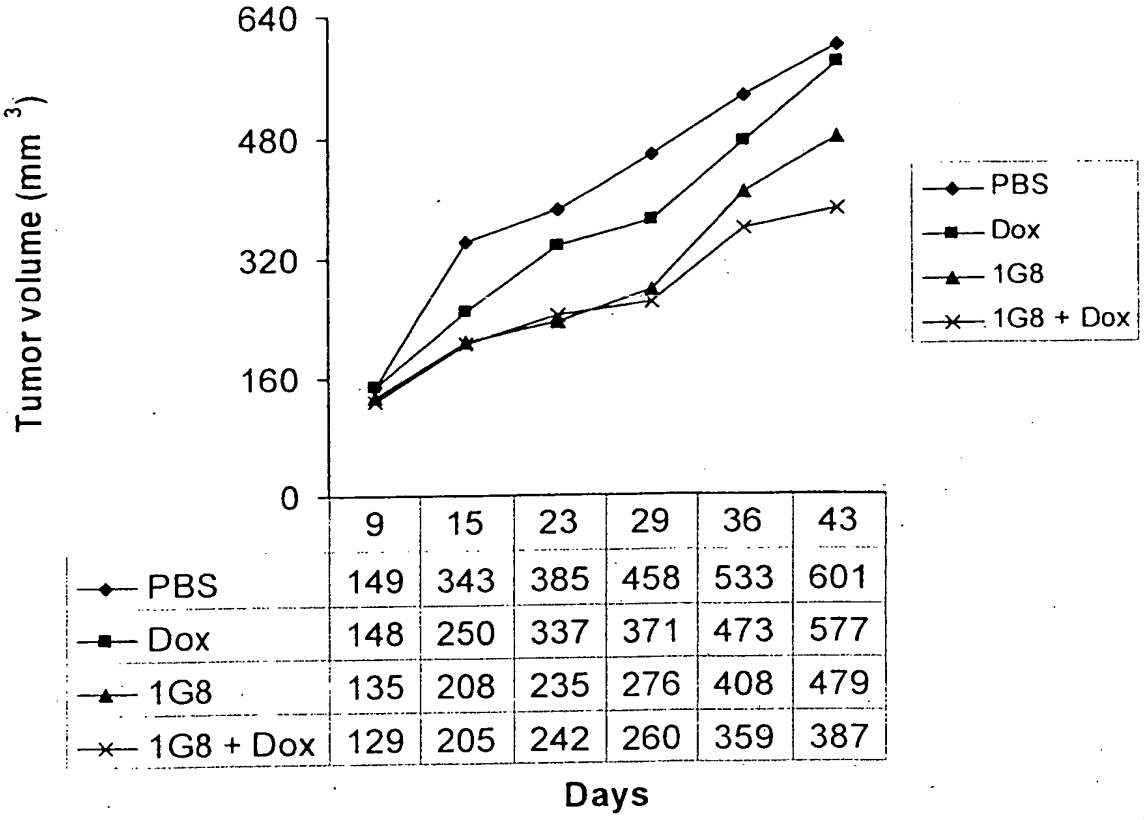
100
80
60
40
20
0
% Survival
0
25
50
75
100
125
Days
PBS
3C5

B)



100
80
60
40
20
0
% Survival
0
10
20
30
40
50
60
70
80
90
Days
PBS
3C5

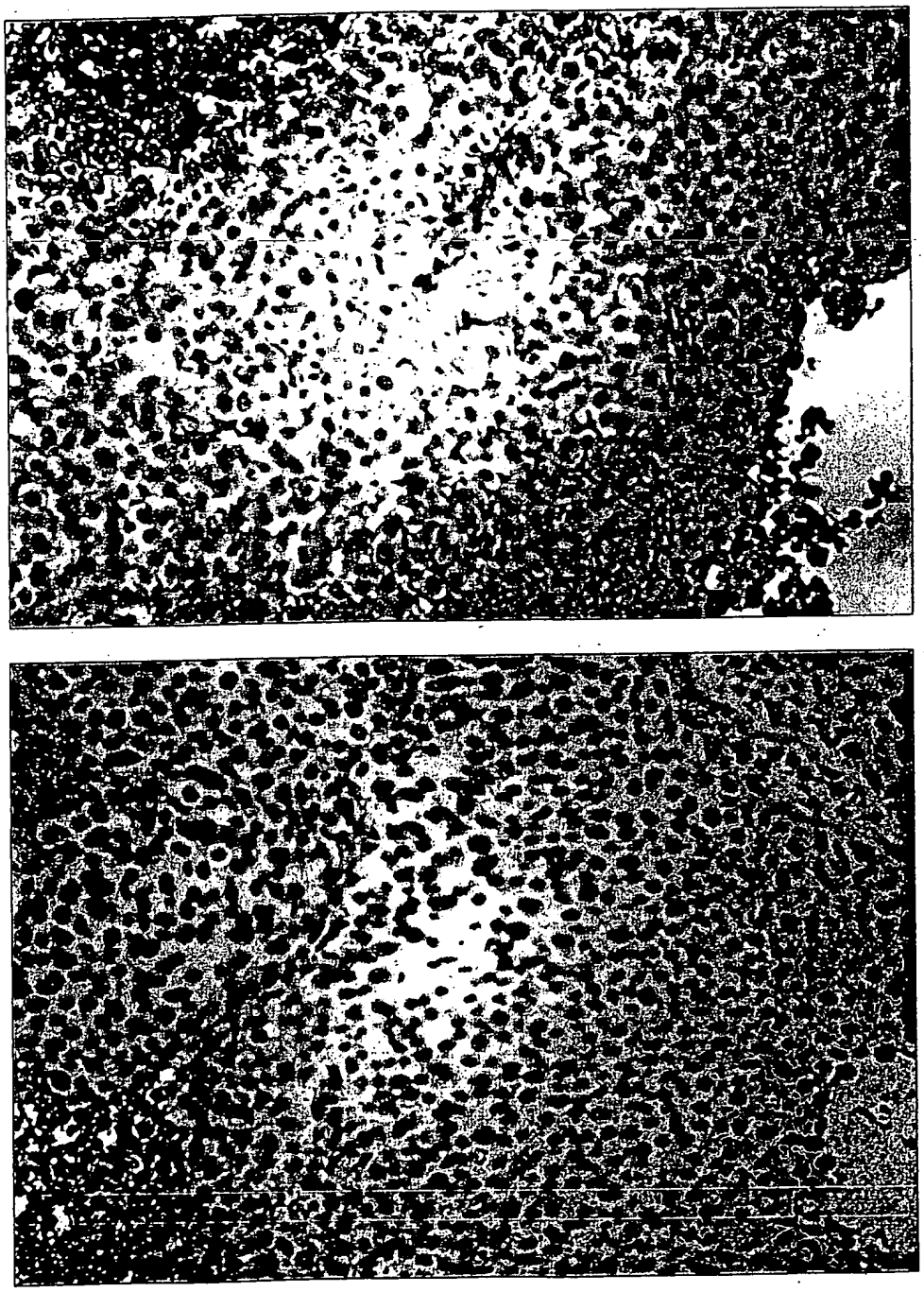
FIG. 70



	9	15	23	29	36	43
PBS	149	343	385	458	533	601
Dox	148	250	337	371	473	577
1G8	135	208	235	276	408	479
1G8 + Dox	129	205	242	260	359	387

Days

FIG. 71



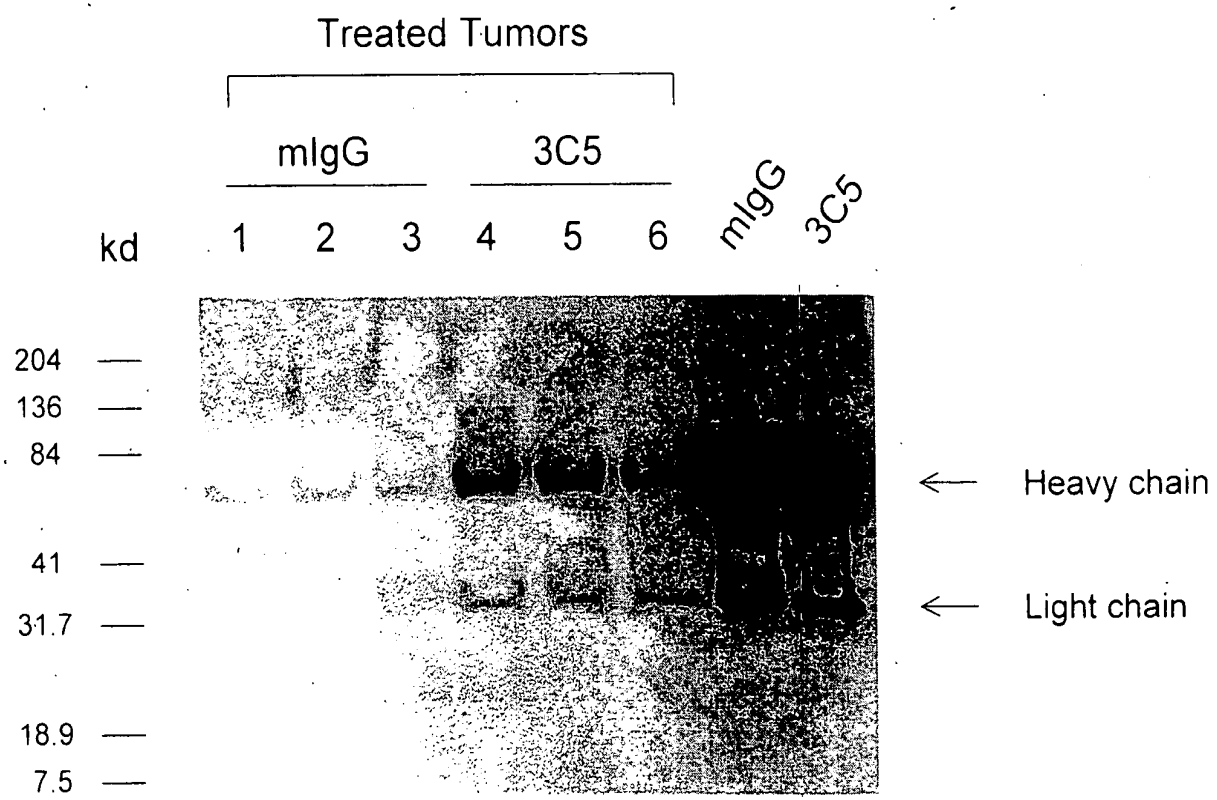


FIG. 72

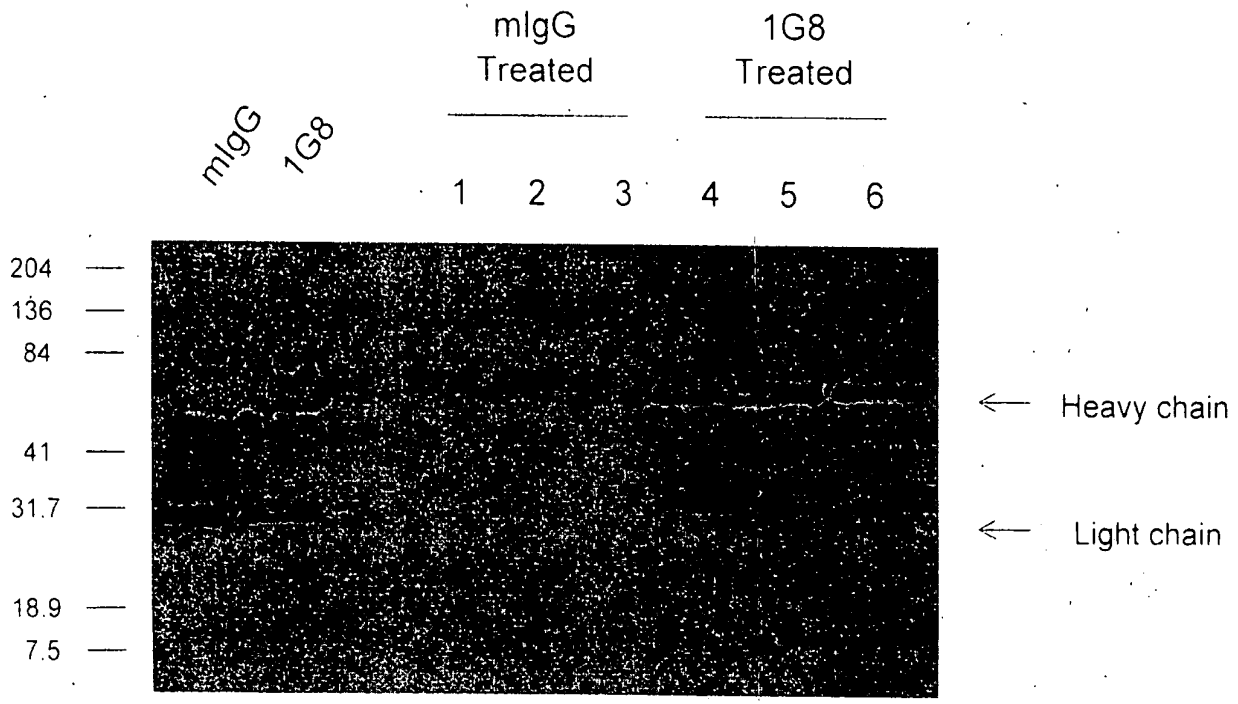


FIG. 73